ANNALS
OF
OTOLOGY, RHINOLOGY
AND
LARYNGOLOGY

VOL. 46 DECEMBER, 1937 No. 4

LXXIV

CHRONIC PROGRESSIVE DEAFNESS FROM A NUTRITIONAL STANDPOINT: A PRELIMINARY REPORT

GRANT SELFRIDGE, M.D.

SAN FRANCISCO

During the past year a group of cases of chronic progressive deafness have been studied from the standpoint of their dietary histories. Some of these individuals have an hereditary history and should, no doubt, be classified as otosclerotics. Common to most of these cases was a definite lowering of all notes below 4096 both for air and bone conduction. Perhaps these are to be labeled as adhesive types and associated with secondary infections (toxins). Their dietary and dental histories, however, indicate definite nutritional disturbances. McCarrison[1] has said, "Nutrition is a fundamental function on which the condition of the body, that is to say, health depends. Faulty food, faulty nutrition, faulty function, faulty structure, faulty health—disease." The purpose of this report is to point out a probable relationship between nutritional deficiencies and chronic progressive deafness.

In the opinion of a few, otosclerosis has not been found to be associated with constitutional factors. Thus Shambaugh[2] says, "A point worth emphasizing is the general health of the patients with otosclerosis. The statement has been made that patients with otosclerosis have a constitutional inferiority. We found that almost without exception these people enjoy excellent health and are men-

tally and physically normal in every respect except for their hearing." Gray[3] makes the statements, "There is no evidence whatsoever of any difference in the bone metabolism of the body. On the contrary, the subjects of otosclerosis are, apart from their deafness, perfectly normal individuals with ordinary average health. The deafness of otosclerosis is to a large extent functional, and is a result of the insufficient supply of blood to all the nerve structures concerned in the perception of sound. The preponderance of women as subjects of otosclerosis is the result of greater instability of the vasomotor system and the more frequent disturbances to which it is exposed."

Individuals with otosclerosis may appear to be in excellent health, yet I am convinced that certain valuable information is to be found in their past histories and particularly their dietary histories. The relationship of dietary factors to health and disease is still in the experimental stage as evidenced by the discoveries in present day literature. Within the next decade it is highly probable that the otologist will find an explanation of some of their problems in this phase of the work.

The rôle that infections play in chronic progressive deafness is uncertain. Fowler[4] has laid stress on infections of the nose, particularly of the post ethmoids in order to explain the periodic drop in the hearing of otosclerotics. It is my contention that many infections of the upper respiratory tract do not usually occur unless the soil is properly prepared. Clauson[5] says, "Resistance to infection may be greatly reduced by deficient diet. A deficiency in diet of vitamin A or C appears quite definitely to lower resistance to infection. In certain cases the lack of vitamin B per se cannot be said to have a proven effect of lowering resistance (such lowering when it occurs is usually due to an associated deficiency of vitamin A). It seems probable that the existence of a partial deficiency (of vitamins) may result in a loss of resistance in infections—." Under deficient diet as mentioned by this author there is included a protein deficiency and a deficiency of certain mineral elements, notably calcium. He believes that a food deficiency deranges the normal production of hormones and the functional perfection of the sympathetic control.

Dietary histories of cases of chronic progressive deafness have been correlated with the blood chemistry studies. The following determinations have been made in each instance; vitamin A, with the visual photometer, blood for vitamin C, calcium, phosphorus, potassium, magnesium, plasma and red blood cell magnesium and sodium, phosphates for vitamin D, total serum protein, serum albumin, serum globulin and the A G ratio, and basal metabolic determinations.

These patients have been given various vitamin concentrates including the B complex. While the series is small these investigations will be continued with the hopes that a larger number of cases will confirm the present findings.

REPORT OF CASES

CASE 1.—Minerva D., age 15. Height 5 feet six inches. Weight 120 pounds. Her physician reports that her general health is very good. Had an abscess in left ear in infancy. Measles at six years; chicken pox at five; German measles one year ago. Subject to slight colds (four or five yearly). There is no deafness in her family. Audiograms of her parents show bone and air conduction normal. First noticed deafness six years ago; more pronounced one year ago.

Tooth History: Mother as a child had soft teeth, today at age of forty has nearly all her teeth out. Patient began to have teeth filled at age of nine, about the time when hearing began to decline; at present has fifteen teeth filled.

Mother's diet during period of gestation was precarious, as to essential foods, due to marked nausea after meals. Her intake of milk especially was very small and it is safe to assume that her B, C and D intake was small. It has been impossible for the mother to give any intelligent answers as to the daughter's diet in infancy and childhood. At the present time her intake of milk, eggs, butter, meat, vegetables, citrus fruits seems to be satisfactory. However, from the age of eight to thirteen years, as a result of restricted family income her intake of all the vitamins was definitely restricted.

Examination of Ears: Both membrana tympani look normal; eustachian tubes also; nose: slightly high deviation of septum; naso-pharynx adhesion vault to left tube. Tonsils out at age of five. Hearing test: right, whisper voice 15 inches; conversation, 24 feet. Left, whisper voice 3 inches; conversational 3 feet. Rinné minus. Lewis fixation plus, right and left.

Laboratory data: Blood count: Hgb., 127 per cent; R. B. C., 5,790,000; W. B. C., 8000; poly., 71 per cent; stab., 3 per cent; lymphs., 25 per cent; monos., 3 per cent; eos., 1 per cent.

Basal metabolic rate is minus 3.3 per cent.

Visual photometer for vitamin A (first and second readings: normal). X-ray of bones; chronological age 16 years; Bone age series: "The bone age corresponds to 18 years. There is no abnormality in bone density or structure."

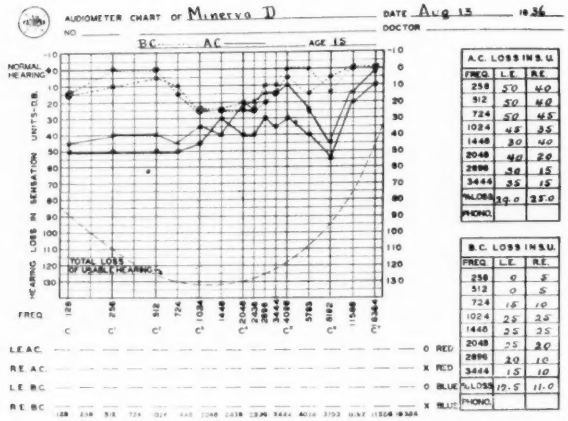


Fig. 1

BLOOD CHEMISTRY

Vitamin C	0.72 mgs.%
Cholesterol	310. mgs. per 100 cc. plasma
Total serum protein	5.54 mgs.% (low normal)
Serum albumin	4.01 mgs.% (low normal)
Serum globulin	1.53 mgs.%
A G Ratio	2.62
Serum calcium	10.5 mgs.%
Diffusible calcium	5.0 mgs.%
Inorganic serum phosphate	3.0 mgs.% (low)
Plasma magnesium	2.6 mgs.% (normal)
R. B. C. magnesium	7.9 mgs% (high normal)
Phosphatase	0.19

CONCLUSION

The serum proteins and phosphorus are low. The serum calcium is relatively and significantly high when compared with the proteins.

Her treatment has included vitamin B complex, alone, for a period, then the addition of the filtrate factors. Also C vitamin acid, 150 mgs. daily, as her C test suggested a low normal. Also thyroid (B. and W.) gr. 1 daily on account of high cholesterol. Dietary: Increase in milk, eggs and foods with a low magnesium content.

CASE 2. Mrs. R., age 36, consulted me November 4, 1934, complaining of deafness, first noticed at the age of eighteen years while

at school. Five years later tinnitus, described as a knocking sound. Hears well on the telephone and better in a train or automobile. Hearing has gradually decreased, especially during the past year (1933). There is no deafness in the family. Has been treated for three years, catheterizing of her eustachian tubes, diathermy for several weeks, without results.

Her regular physician reports no organic trouble. Her fear senses have been exaggerated more or less since childhood. Has always been extremely nervous, since twelve years old. In recent years has complained considerably of fatigue.

Nose normal, throat also. Tonsils out. Ear drums appear normal, eustachian tubes perhaps a trifle narrow. Tooth history is one of the soft type, easily decaying, and many fillings in her childhood period. Better in recent years.

A dietary study was made by Nina Simmonds, a summary of which is as follows:

Consumption of milk has been low all her life. Cereals also. Had plenty of butter and cod liver oil in early life. Later a sufficient amount of vegetables and fruit. Meats and eggs not normal. Her vitamins: A low, B low all her life, C fair, G fair, calcium and phosphorus low.

Blood Studies (July, 1934): Total calcium 9.75 mgs.; diffusible 4.20 mgs.; inorganic phosphates 3.65 mgs.; potassium 17.8 mgs. (normal).

Blood Studies (March, 1937): Vitamin C—0.76 (low side of normal); sodium 331; potassium 23.8; K Na ratio 16.1 calcium 10; phosphorus 4.7; Ca P ratio 2.1; magnesium 1.52; cholesterol 200; phosphatase 0.11.

Treatment: She was given Furstenberg's ammonia chloride and salt free diet for several weeks without result. Then the vitamin B complex from February, 1935, to June, 1936, several courses of ten injections of cortical extract during the year 1935-1936 with complete relief of her fatigue and apparently marked improvement in her fear senses. No medicine from June until September, 1936. At this time she was given the B complex, one teaspoonful three times a day with an additional dose of six teaspoonsful daily of the filtrate factor (the complex contains 50 I. U. of B_1, 10 Sherman units of B_2, 20 units filtrate factor per cubic centimeter. The filtrate factor syrup contains 20 units per cubic centimeter of 80 per teaspoonful.

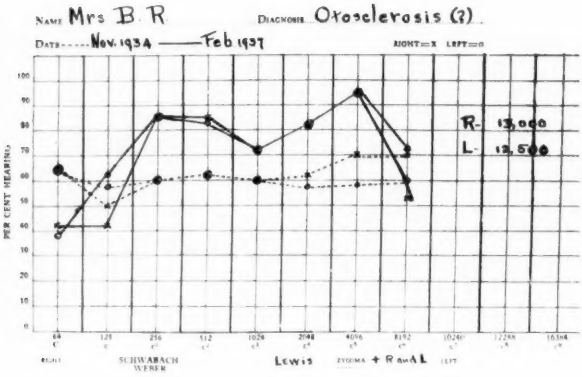

NAME Mrs B R
DIAGNOSIS Otosclerosis (?)
DATE---- Nov. 1934 —— Feb 1937
RIGHT = X LEFT = O
PER CENT HEARING
R- 13,000
L- 12,500
SCHWABACH
WEBER
LEWIS
ZYGOMA + RomAL

Fig. 2

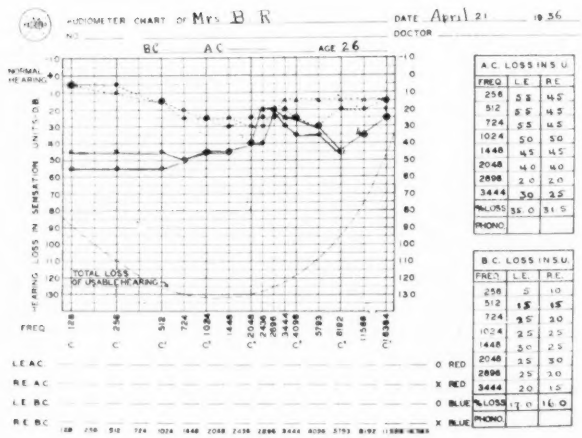

AUDIOMETER CHART OF Mrs B R
DATE April 21 1936
DOCTOR
BC AC AGE 26
HEARING LOSS IN SENSATION UNITS O.B.
TOTAL LOSS OF USABLE HEARING
FREQ
A.C. LOSS IN S.U.
FREQ L.E. R.E.
256 55 45
512 55 45
724 55 45
1024 50 50
1448 45 45
2048 40 40
2896 20 20
3444 30 25
%LOSS 35.0 31.5
PHONO
B.C. LOSS IN S.U.
FREQ L.E. R.E.
256 5 10
512 15 15
724 25 20
1024 25 25
1448 30 25
2048 25 30
2896 25 20
3444 20 15
%LOSS 17.0 16.0
PHONO
L.E. A.C. O RED
R.E. A.C. X RED
L.E. B.C. O BLUE
R.E. B.C. X BLUE

Fig. 3

Audiogram No. 1 shows change in curve from November, 1934, to February 24, 1937.

Audiogram No. 2 shows change from October 21, 1936, to February 24, 1937, during which time only the filtrate factor was taken.

When first seen in 1934 I had to raise my voice quite considerably to make her hear. She was unable to hear the whispered voice. At the present time, April, 1937, she hears conversational voice at 27 feet. Whispered voice at six feet.

COMMENT

It would seem from the above study that there has been a steady improvement in her hearing. I am mindful that meteorological factors and fatigue do influence the hearing, but she has been checked and rechecked so many times in different weathers, I'm inclined to believe the improvement is the result of treatment, rather than due to environmental factors.

CASE 3.—Dr. S. McM., age 36. Height 5 feet 7 inches. Weight 155 pounds. Born in Glasgow, Scotland, December, 1899. Lived in Scotland until age of three years, then in Canada on a wheat ranch for three years; back to Scotland for one and a half years; back to Canada for another three years, then to South Africa for three years. At the end of that time he was twelve years old. These journeyings are important because of the probable bearing on his dietary history during that period.

It seems probable from what is known of the limitations of the Scotch and English dietary at that period that the excess of oatmeal porridge, white flour, lack of fruits and vegetables, and especially citrus fruits, prior to the age of twelve, had a definite influence on his subsequent ear involvement.

Deafness in family: father at age of forty-five, thought to follow erysipelas. No other member of family.

Patient had whooping cough at five years of age and measles in 1916, and noticed then his beginning deafness. Had influenza in 1918. In 1931 had a throat infection and says, following that incident, his hearing was lower. After this his tonsils were removed. Following the operation he was given vaccines and thinks his hearing was somewhat improved as a result.

He consulted the late Dr. Albert Gray of London, England, in 1912, who diagnosed his deafness as otosclerosis. Several other otologists have concurred in Gray's opinion.

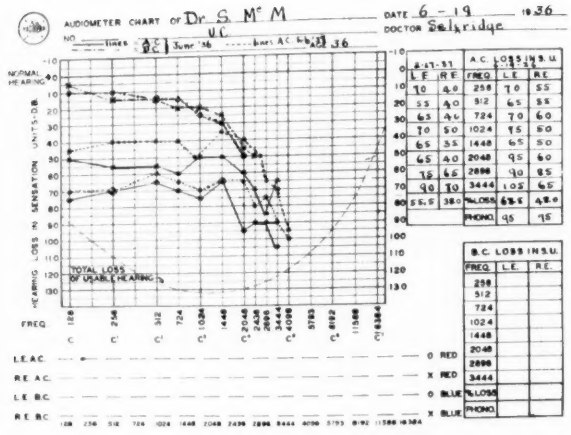


Fig. 4

Examination of ears, nose and throat shows nothing of importance. Mt. appears normal. Tubes are open.

The laboratory studies are as follows:

Blood count: Hgb., 98 per cent (Sahli); R. B. C., 4,940,000; W. B. C., 3,300; polys., 29.1 per cent; lymphs., 49.6 per cent; mononuclears, 15 per cent; eosinophiles, 6 per cent; basophiles; 3 per cent. Red cells and platelets are normal.

Basal metabolic rate was 17.1 per cent minus.

Vitamin C—0.15.

BLOOD CHEMISTRY

	Cholesterol	182	mgs. %
(Xo	Total Serum Calcium	11.2	mgs.
(	Serum Potassium	24.8	mgs.
(	Serum Sodium	503.	mgs.
(	Plasma Magnesium	2.35	mgs.
6.2 - 7.2 (Xo	R. B. C. Magnesium	8.40	mgs.
	Hematocrit (Vol. packed R. B. C.)	46.	mgs.
o	Serum inorganic phosphorus	3.8	mgs.
	Total serum protein	5.98	gms. %
	Serum Albumin	5.	gms.
o	Serum Globulin	0.95	gms.
	Phosphatase	1.5	units

Treatment: This patient has been taking, daily, rice bran B complex with an addition of the filtrate factors of the B complex, from October, 1936, to April, 1937.

Beginning June 1, 1937, and based on the laboratory findings, at the suggestion of Dr. Salvatore Lucia of the University of California Medical School, who has been responsible for these various laboratory checks, the following treatment has been advised:

1. Acid ash diet, with low magnesium foods.

2. Ammonium chloride (enteric coated) grs. 15 t.i.d.

3. Extr. Thyroid (Armours) beginning gr. 1 daily.

4. Continue B_1 complex or B_2 complex when available.

5. Vitamin C, 300 mgs. daily for one month (then recheck blood).

Whether the following suggestions will result in further improving his hearing or will result in preventing a further decline in his hearing, time only will tell.

Case 4.—Miss Z. L., age 36 years. Diagnosis: otosclerosis, by two well-known otologists.

The outstanding facts about this patient are:

1. Deafness beginning about the age of puberty. No hereditary history of deafness, other than a cousin on the father's side, who is said to have the same type of deafness.

2. She was a November baby, born on a farm in Minnesota and probably, according to Simmonds' report, had infantile rickets before she was four months old. A bad nutritional history most of her life.

3. Marked vasomotor instability.

4. A suggestion, as reported by her physician, Dr. Ernest Falconer, of hypofunction of pituitary, and also some evidence favoring thyroid hypofunction. He says: "I am inclined to regard the thyroid hypofunction as being primarily due to a deficiency of the thyrotrophic substance of the pituitary gland."

Her basal metabolic rate was minus 23 per cent. He thinks she, "had a functional hyperactivity of the pituitary in the past, possibly in childhood and early adolescence, but that now there is an exhaustion or low pituitary function, leading to a general asthenia, as is shown in her low blood pressure, which seven years ago was

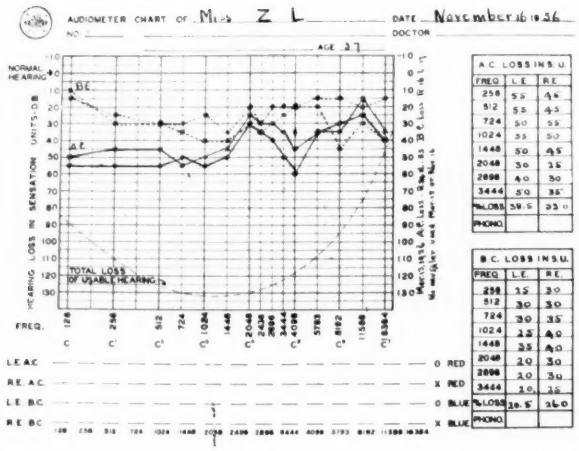

AUDIOMETER CHART OF Miss Z L
DATE November 16 1926
NO
DOCTOR
AGE 37
NORMAL HEARING
HEARING LOSS IN SENSATION UNITS O.B.
B.C.
A.E.
TOTAL LOSS OF USABLE HEARING
FREQ.
LE A.C.
RE A.C.
LE B.C.
RE B.C.
0 RED
X RED
0 BLUE
X BLUE
A.C. LOSS IN S.U.
FREQ. L.E. R.E.
256 55 45
512 55 45
724 50 55
1024 35 50
1448 50 45
2048 30 25
2896 40 30
3444 30 35
%LOSS 39.5 33.0
PHONO.
B.C. LOSS IN S.U.
FREQ. L.E. R.E.
256 15 30
512 30 30
724 30 35
1024 25 40
1448 35 40
2048 20 30
2896 20 30
3444 20 25
%LOSS 20.5 26.0
PHONO.

Fig. 5

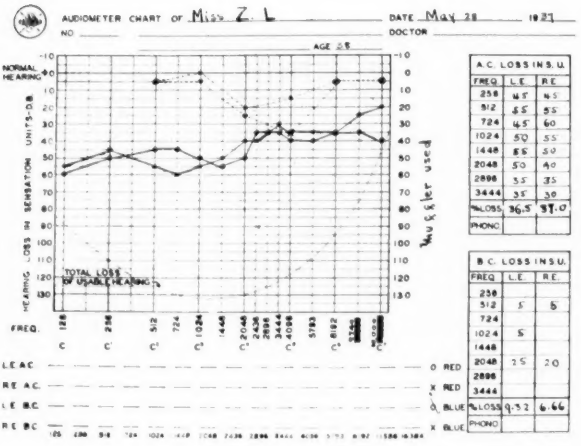

AUDIOMETER CHART OF Miss Z. L
DATE May 28 1927
NO
DOCTOR
AGE 28
NORMAL HEARING
HEARING LOSS IN SENSATION UNITS O.B.
Watkler used
TOTAL LOSS OF USABLE HEARING
FREQ.
LE A.C.
RE A.C.
LE B.C.
RE B.C.
0 RED
X RED
0 BLUE
X BLUE
A.C. LOSS IN S.U.
FREQ. L.E. R.E.
256 45 45
512 55 55
724 45 60
1024 50 55
1448 55 50
2048 50 40
2896 55 35
3444 35 30
%LOSS 36.5 37.0
PHONO.
B.C. LOSS IN S.U.
FREQ. L.E. R.E.
256
512 5 5
724
1024 5
1448
2048 25 20
2896
3444
%LOSS 9.52 6.66
PHONO.

Fig. 6

80 50. In 1933 it was 95/60. Low blood sugar (68.9 mg.); low hemoglobin 76 per cent.

Her nutritional study by Dr. Nina Simmonds, is as follows: Since twenty years of age, the carbohydrate intake has been fair, fats fair, protein low. The calcium intake is low, phosphorus fair; copper and iron, questionable. Vitamins: A is low; B is low; C, low to fair D, low; G, possibly sufficient. Acid-alkaline ash, probably acid. The electrolytes: Calcium, 9.9; phosphorus, 3.6; potassium, 16.95.

During the period prior to March 3, 1936, the only treatment given this patient was thyroid extract and a correction of her dietary errors. From March 3, 1936, to September, 1936, she was given the B complex made from rice bran. No apparent change in audiograms, although she thought her hearing for voice was improved. Audiogram May 8 shows change in bone conduction.

One night in September, 1936, she went to a movie, sat in her usual place, and while there, without using her hearing device was able to hear the entire performance. On leaving the theater, she was knocked down by an automobile, receiving a head injury. Was confined to bed several days and for some time was unable to hear, a condition probably the result of shock.

Prior to this her medication was changed to the filtrate factors and continued until about April 1, 1937.

Laboratory studies around June 1, 1937, as follows:

Basal metabolic rate: minus 21 per cent.

Visual photometer reading for vitamin A showed a high excess.

Blood vitamin C—2.10 mgs. per cent.

BLOOD CHEMISTRY

Cholesterol	276.	mgs.%
Serum Sodium	273.	mgs.%
Serum Potassium	23.4	mgs.%
Na K ratio	11.7	
Calcium	10.0	mgs.%
Diffusible calcium	4.3	mgs.%
Phosphorus	3.6	mgs.%
Ca P ratio	2.8	
Red Blood Cell Magnesium	5.5	mgs.%
Phosphatase	.34	units% plasma
Serum Albumin	4.6	gms.%
Serum Globulin	2.6	gms.%

It will be seen from these audiograms that there is a definite improvement in bone conduction, and a slight improvement in air conduction in the left ear, a loss in the right. Whether the loss in that ear can be attributed to her injury is an open question.

CASE 5. Miss Freda S., age 41 years. Height 5 feet 3 inches. Lateral type of body build. Weight 155 pounds.

Principal complaints, deafness, chronic constipation, recurrent colds. No deafness in family. At age of twenty-six noticed beginning difficulty in hearing; gradual progress of deafness, at a standstill for some time. Does not hear better in a noise. Is confused when several people are talking.

Tooth history: very bad teeth as a child. First teeth decayed readily. When permanent teeth came in they were soft and decayed readily. Has had four extracted, and all the rest are fillled. Began going to the dentist at age of thirteen. Grandparents and parents had very bad teeth.

Dietary history is exceedingly bad, and has always been so, due to ignorance, and a poor economic situation. No milk or eggs, leafy vegetables or citrus fruits. Hence deficiency in all vitamins.

Examination of nose: deflection of septum; intra-nasal opening of both antra; tonsils present.

Ears: both mt. move in anterior post areas. Malles appear fixed. Tubes open.

Hearing: whispered voice for right ear 3 inches; for left 3 inches. Conversational voice for right ear 12 feet; for left 9 feet. Rinné minus. Lewis fixation plus right and left minus.

Laboratory studies: Blood count: Hgb., 60 per cent; R. B. C., 3,990,000; W. B. C., 7700; polys., 67; lymphs., 30; monos., 2; eos., 1. Red cells show slight achromia and slight aniscocytosis.

Basal metabolic rate: minus 10 per cent.

Visual photometer shows a slight deficiency for A; vitamin C is 0.5 mgs. per cent (low); photophatases 0.073.

Treatment: This patient was given the filtrate factors* made from rice bran on October 16, 1936, one-half ounce night and morning, and continued for several weeks, when the dose was reduced one-half and continued until about April 15, 1937.

*Since the report of these cases was written, it has been learned that the filtrate factors were not entirely freed of B_1.

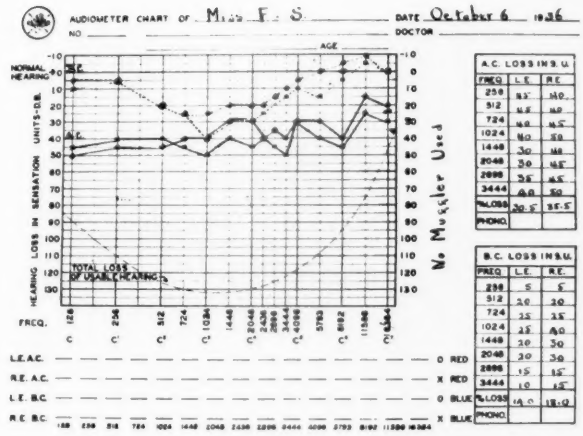

AUDIOMETER CHART OF Miss F. S.
DATE October 6 1926
NO.
DOCTOR
AGE
NORMAL HEARING
HEARING LOSS IN SENSATION UNITS-DB.
B.C.
A.C.
TOTAL LOSS OF USABLE HEARING
No Muffler Used
FREQ.
L.E. A.C.
R.E. A.C.
L.E. B.C.
R.E. B.C.
RED
BLUE
A.C. LOSS IN S.U.
FREQ L.E. R.E.
256 25 40
512 45 40
724 40 45
1024 40 50
1448 30 40
2048 30 45
2896 35 45
3444 40 50
%LOSS 30.5 35.5
PHONO.
B.C. LOSS IN S.U.
FREQ L.E. R.E.
256 5 5
512 20 20
724 25 25
1024 25 40
1448 30 30
2048 30 30
2896 15 15
3444 10 15
%LOSS 14.0 18.0
PHONO.

Fig. 7

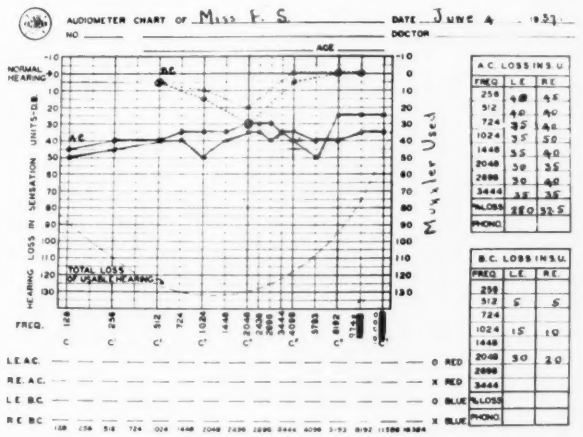

AUDIOMETER CHART OF Miss F. S.
DATE June 4 1927
NO.
DOCTOR
AGE
NORMAL HEARING
HEARING LOSS IN SENSATION UNITS-DB.
B.C.
A.C.
TOTAL LOSS OF USABLE HEARING
Muffler Used
FREQ.
L.E. A.C.
R.E. A.C.
L.E. B.C.
R.E. B.C.
RED
BLUE
A.C. LOSS IN S.U.
FREQ L.E. R.E.
256 45 45
512 40 40
724 35 40
1024 35 50
1448 35 40
2048 30 35
2896 30 40
3444 35 35
%LOSS 33.0 32.5
PHONO.
B.C. LOSS IN S.U.
FREQ L.E. R.E.
256
512 5 5
724
1024 15 10
1448
2048 30 20
2896
3444
%LOSS
PHONO.

Fig. 8

BLOOD CHEMISTRY

Sodium	334.	mgs.%
Potassium	23.8	mgs.%
Na K ratio	16.1	
Calcium	10.9	mgs.%
Phosphorus	2.62	mgs.%
Ca P ratio	4.16	mgs.%
Magnesium	1.72	mgs.%
Cholesterol	169.	mgs.%
Calcium diffusible	4.5	mgs.%
R. B. C. Magnesium	6.4	mgs.%
Serum Albumin	4.4	gms.%
Serum Globulin	2.1	gms.%
A G ratio	2.0	gms.%

C-vitamic acid, 300 mgs. daily was added April 10 for one week, at which time the dose was reduced one-half and is being continued.

April 24, Navitol capsules (Squibbs A and D), one after meals. She is therefore taking vitamin A, B, C, D—in addition to foods containing these substances.

As a result her general health is much improved, the constipation has disappeared, no colds during the past winter and says she feels better than she has in years. During this period the hemoglobin has improved and her blood count June 5, 1937, is as follows: Hgb., 71 per cent; R. B. C., 4,290,000; W. B. C., 5200; polys., 62 per cent; lymphs., 37 per cent; eosins., 1 per cent. Red cells show slight achromia.

These preliminary studies indicate that more than one factor may be involved in chronic progressive deafness. A vitamin C deficiency may initiate metabolic disturbances in the bone if there is a lack of optimal calcium and phosphorous intake. Rinehart[6] described for vitamin C deficient guinea pigs a decalcifying process of bone, in the ends of the long bones. In the joints there was first an increase of fluid which was followed by the formation of fibrous issue. The feeding of C vitamic acid to these animals tended to restore to normal the appearance of the long bones and also caused the fibrous tissue to disappear. Seminov[7] has found allergy and the lack of vitamin C to be important factors in adhesive deafness. He says, "that hyperplastic otitis media is characterized by epithelial and mesenchymal proliferation," and specifically as, "being related to vitamin deficiency and hypersensitive reaction (allergy) of infants." He further states, "ten per cent of the infants examined had evidence of rickets," and further on, "vitamin C deficiency may

be linked with faulty development of mesenchyme which may or may not appear in connection with vitamins A and D disturbances (rickets, etc.)." Guggenheim[8] reported a normal case of resorption of mesenchyme in which there was later an infection of the ear with no deafness. Another case in which the mesenchyme was not absorbed and in which an infection followed; marked fibrosis and deafness resulted. One wonders what the vitamin C content of the blood might have been in these cases.

Becks[9] studied one hundred cases of root resorption of the teeth and found definite faulty nutritional histories. They showed a disturbance of the Ca P ratio and low vitamins C and D diets. Twenty-three had basal metabolic rates below minus 15 per cent.

T. Ono[10] reported experimental C avitamosis in relation to the ear. Briefly stated, he found a thickening of the ear drum and middle ear mucosa, hemorrhages in the middle ear, atrophy of the tensor tympani muscle. In the bony tissue, external canal, ossicles and proximity, evidences of decalcification, dilatation of the bony canaliculæ tumefaction of the connective tissue cells, formation of osteophytes, fibrous marrow, etc.; in the inner ear, he described hemorrhages and edema of Corti's organ.

Until recently the vitamin B complex has been known as B_1B_2. Today the B complex is called B_1, and the B_2 complex. Elvehjem, Gyorgy, Kocher, Lepkovsky and Jukes[11] have divided the latter into three components: flavine (the rat antiacrodynia); B_6 factor, and the filtrate or chick antidermatitis factor. There is already an impression that the filtrate factor may contain one or more components. Jukes says, "the name filtrate factor is not proposed as a permanent title for the vitamin, but is used for the sake of brevity and specificity."

McCarrison[1] believes this vitamin affects every part of the body, the hair, skin and nails, the muscular and bony system, the general and autonomic nervous system, the cardio-vascular system, mucous membranes, particularly of the intestinal tract.

I used the B complex made from California rice bran in cases of high tone loss, because it contained all the different factors of the B complex, i. e., $B_1B_2B_6$ and the filtrate factors. The conclusions from these studies are that in the early cases, with beginning loss, the use of B_1 in solution containing 500 I. U., correcting the dietary errors and including a plentiful amount of B foods, is sufficient to restore most of the hearing. In those cases where the loss extends to 1024 cycles, the entire B_2 complex should be used. I have also used, on the early cases, the B_1B_2 absorbate of Lilly and Company, and a

similar but more potent preparation furnished by the makers of rice bran products. In the remainder of the cases of high tone loss the B complex syrup was given. The results with audiograms of fourteen cases appeared in the March, 1937, issue of this journal.

In relation to the changes in the nerve observed in chronic progressive deafness where the hearing loss is 25 per cent and over, it seems advisable to use a preparation containing only the B_2 complex, i. e., flavin (or B_2) B_6 and the filtrate factors, because recent studies of Covell, to be published shortly, indicate that flavin deficient chicks present the same amount of demyelinization as found in B_6 deficient rats, and chicks deficient in the filtrate factors.

That the filtrate factors may prove more important is supported by the recently reported cure of four cases of true human pellagra by Fonts, Lepkovsky, Helmer and Jukes.[12]

The similarity between Paget's, Recklinghausen's disease and otosclerosis has been pointed out (Weber, Nager and others).

Gill,[13] discussing bone metabolism, says, "the local factors which influence bone metabolism are: first, the hydrogen ion concentration and the carbon dioxide tension of the plasma; second, the presence of substances which may influence the solubility of calcium phosphate, such as proteins and the salts of magnesium, and third, phosphatase and possibly yet unrecognized enzymes."

Speaking of Paget's disease he says, "the blood chemistry is normal except for a high phosphatase content." He treats these cases with "a diet low in calcium, low in phosphorus and high in magnesium. The latter is given as magnesium carbonate in dosages of four to ten grams per day."

He believes decalcification may be caused primarily by an inadequate dietary and vitamin intake, low calcium and high phosphorus, or low phosphorus and high calcium with low vitamin D in both; secondly, by hypersecretion of para-thyroid hormone, and thirdly, by the administration of such elements as magnesium and strontium. Ammonium chloride is another factor.

He also says that the disease may be controlled by a diet rich in calcium and phosphorus, such as milk, cheese, meats (including fish), also calcium and dicalcium phosphate. Likewise vitamin D in the form of 250 D Viosterol, 30 to 60 drops.

A relationship between the various vitamins, ductless glands and electrolytes is not to be overlooked.

The relationship of vitamin A to the thyroid has been pointed out by Schmidt.[15] B has been said to be related to the pituitary (Evans)[14] as also to the adrenal cortex (Hartman).[15] In B deficiency Bodansky[16] finds a depressed gastric and pancreatic secretion accompanied by a reduced enzymatic activity (phosphatases).

C is probably related to the adrenal cortex (Hartman),[17] D to the parathyroids (Schmidt)[18] and E has a relation to the sex hormones (Evans).[19]

It is also well known that the absence of B produces an atrophy of the pituitary as well as all the other glands (C. Funk and D. Mackenzie quoted by Zondek).[20] and Grollman.[21]

The parathyroids, thyroid and the anterior lobe of the pituitary are all concerned in calcium metabolism (Schmidt).[22] Schmidt and Greenberg have called attention to the value of diffusible calcium determination, stating that a low determination indicates hypoparathyroidism, a high reading indicates hyperparathyroidism.

Potassium and sodium are definitely related to the cortex, magnesium to the parathyroids, and perhaps to the cortex (Greenberg).[24]

In a series of cases of otosclerosis studied by Fowler, he found the amounts of calcium and phosphorus to be within the normal range, as was the calcium-phosphorus ratio in the work of Crockett and Aub.

On the other hand the experimental work of Becks and Weber,[25] Beck's[9] studies on tooth resorption, Gill's[13] studies on bone metabolism, Freyburg's[26] work on hypoparathyroidism, indicate definitely, when the calcium phosphorus ratio is out of line, definite evidence of bone changes, i. e., decalcification does occur. Eddy and Dalldorf[27] call particular attention to the decalcification in the teeth and bones in experimental animals and humans as a result of diets deficient in vitamin C.

COMMENTS

These five cases of chronic progressive deafness indicate that they are not normal individuals. It also appears that some of them are definitely aided by the use of vitamin concentrates. There remains to be studied further the use of these and similar concentrates in other cases and to observe the present cases over a period of years. The findings of Covell for the peripheral auditory mechanism of dietary deficient animals should prove of interest. While experimental studies aid in confirming or disproving results of this nature, it must be borne in mind that there is a difference between the experimentally induced deficiency and the milder type of deficiency encountered in clinical cases, such as the ones described.

Gray may not have been wrong when he considered the nerve involvement of otosclerotics as primary and the bone changes as secondary, if an explanation is attempted from a nutritional standpoint. If the lack of vitamins of the B complex (the most obvious deficiency in the human dietary today) can explain the changes in the nerve and the vaso-motor mechanism (McCarrison) then it is probable that a lack of vitamin C might explain changes in bone metabolism. Such an hypothesis may be incorrect since considerable information is needed before inter-relationships of the way in which vitamins, ductless glands and electrolytes control body metabolism, is thoroughly understood. Nevertheless it is obvious that dietary disturbances play an important role in otological problems.

LABORATORY METHODS USED AND NORMAL READINGS

Vitamin C:

Normal Reading: 0.7 - 0.9 mgs. per cent plasma (optimum levels above this range).

Method: Farmer, C. J., and Abt.: Proc. Exp. Biol. and Med., 32, 1625 (1933). Abt, A. F., Farmer C. J., and Epstein, T. M.: Jour. Pediat., 8:1. (1936).

Calcium, Total Serum:

Normal Reading: 9.0 - 11.0 mgs. /100 cc.

Method: Clark-Collip, Modification of Kramer-Tisdall Method: Jour. Biol. Chemistry: 110:95 (1935).

Calcium, Diffusible:

Normal Reading: 4.5 - 5.5 mgs. /100 cc. serum.

Method: Greenberg, D. M., and Gunther, L.: Journ. Biol. Chemistry: 85:491 (1930).

Phosphate (as P):

Normal Reading: 3.0 - 4.0 mgs. per 100 cc. serum.

Method: Fiske and Subbarow: Jour. Biol. Chemistry, 66:376 (1925).

Potassium:

Normal Reading: 16.0-22.0 mgs. /100 cc. serum.

Method: Jacobs and Hoffman: Jour. Biol. Chemistry, 93:685 (1931).

Magnesium of Red Corpuscles:

Normal Reading: 5.0-7.5 mgs. /100 cc. cells.

Method: Modified for corpuscles from that of Denis: Journ. Biol. Chemistry, 52:411 (1922).

Sodium:

Normal Reading: 300 - 370 mgs. / 100 cc. serum.

Method: Weinbach, A. P.: Journ. Biol. Chemistry, 110:95 (1935).

Phosphatase:

Normal Reading: 0.1-0.21 phosphatase units / cc. of plasma.

Definition of Phosphatase Unit:

A plasma sample containing one unit of phosphatase per cc. is one of which one cc. will liberate one mg. of inorganic phosphate (expressed as P) from excess of beta-glycero-phosphate solution in 48 hours at 38 degrees C. at pH 7.6, the hydrolysis being carried out in absence of added buffer and other conditions as defined in the article. Can go above 3.0 units in certain generalized bone diseases, osteitis deformans, generalized osteitis fibrosis, osteomalacia and rickets (infantile, adolescent and renal).

Method: Kay: Jour. Biol. Chemistry, 89:235 (1930).

Cholesterol:

Normal Reading: Average normal 150-190 mgs. / 100 cc. serum.

Method: Drekter, I. J., Bernhard, A., and Leopold, J. S.: Journ. Biol. Chemistry, 110:541 (1935).

Serum Proteins: Albumin and Globulin:

Normal Reading: Albumin: 4.5-6.7 gms.% / 100 cc. Globulin: 1.2-2.3 gms.% / 100 cc.

Method: Greenberg, D. M.: Journ. Biol. Chemistry, 82:545 (1929).

REFERENCES

1. McCarrison, Maj. Gen. Sir Robt.: Nutrition in Health and Disease. Brit. Med. J., pp. 611-614 (Sept. 26), 1936.

2. Shambaugh, Geo., Jr.: Severe Deafness in Adults. Arch. Otolaryng., 18: 430-438 (Oct.), 1933.

3. Gray, Albert: The Otosclerosis Problem. J. Laryng. and Otol., 49:629-655 (Oct.), 1934.

4. Fowler, E. P.: Otosclerosis with Other Lesions. Trans. Am. Otolog. Soc., pp. 168, 174, 1933.

Fowler, E. P., Jr.: Otosclerosis and Ultra Violet Light. Trans. Am. Otolog. Soc., p. 75, 1934.

5. Clauson, quoted by McCarrison: Brit. Med. J., pp. 611-614 (Sept. 26), 1936.

6. Rinehart, J. F.: Studies Relating to Vitamin C Deficiency, to Rheumatic Fever and Rheumatic Arthritis; Experimental, Clinical and General Conditions. Annals Int. Med., Vol. 9, No. 6:671-689 (Dec.), 1935.

7. Seminov, H.: Some Observations on the Histopathology of Inflammation of the Eustachian Tube and Middle Ear. Trans. Am. Rhin. Laryng. and Otol. Soc., pp. 563-598, 1936.

8. Guggenheim, L.: Abstract of discussion at Chicago Laryngological and Otological Society. Arch. Otolaryng., 24:804-808 (Dec.), 1936.

9. Becks, H.: Root Resorptions and Their Relation to Pathological Bone Formation. Intern. J. of Orthodonia and Oral Surgery, Vol. 22, No. 3:445 (May), 1936.

Becks, H.: Dental Caries and Paradental Disturbance, Importance of an Adequate Diet for Health of Teeth and Paradenta. J. Am. Dental Assoc., 21:1724-1738 (Oct.), 1935.

10. Ono, T.: Experimental Histopathological Studies of the Ears in A, B and C Avitaminosis. Trans. Jap. Path. Soc., 18:172 (Jan.), 1928.

11. Lepkovsky, S., and Jukes, T. H.: J. Biol. Chem., pp. 109-114, 1936. Lepkovsky, S.: Jukes, T. H., and Krause, M. E.: J. Biol. Chem., p. 115, 1936.

12. Fonts, P. J.; Lepkovsky, S.; Helmer, O. M., and Jukes, T. H.: Proc. Soc. Exp. Biol., p. 245, 1936

13. Gill, H. B., and Stein, T.: Bone Metabolism. J. Bone and Joint Surgery, 18:941 (Oct.), 1936.

14 (19). Evans, Prof. Herbert M.: Personal Communications.

15 (17). Hartman, F.: Studies in Function of Clinical Use of Cortin. Annals Int. Med., 7:6-22 (July), 1933.

16. Bodansky, M.: Introduction to Physiological Chemistry. John Wiley & Sons (3rd Edition), p. 58.

18. Schmidt, Prof. C. L. A.: Personal Communication.

20. Zondek, H.: Diseases of Endocrine Glands. Wm. Wood & Co., pp. 92-93, 1933.

21. Grollman, A.: The Adrenals. Williams & Wilkins, p. 293, 1936.

22 (23). Schmidt, Prof. C. L. A., and Greenberg, L.: Occurrence, Transport and Regulation of Calcium, Magnesium, Phosphorus in the Animal Organism. Physiological Review, 16:298-435 (July), 1935.

24. Greenberg, L.: Personal Communication.

25. Becks, H., and Weber, M.: The Influence of Diet on the Bone System with Special Reference to the Alveolar Process and Labyrinthine Capsule. J. Am. Dental Assoc., 28:197-264 (Feb.), 1931.

26. Freyberg, R. H.: Hypoparathyroidism. J. A. M. A., p. 1773 (Nov. 28), 1936.

27. Eddy, W. H., and Dalldorf, G.: Avitaminosis. Williams & Wilkins, 1937.

LXXV

THE SIGNIFICANCE OF MYELIN SHEATH DEGENERATION FOR THE COCHLEAR NERVE*

W. P. Covell, M.D.
AND
L. Noble

San Francisco

An attempt to determine the significance of certain histopathological changes within the various structures of the cochlea and the cochlear nerve has resulted in the use of different experimental agents. A cytological study of the effects of drugs on the cochlea (Covell)[1] has shown the external hair cells, the external sulcus cells and also those of the stria vascularis to be susceptible to the action of such drugs as quinine and sodium salicylate. The present study is a continuation of the drug effects and also includes the effects of a bacterial toxin and certain dietary factors on the cochlear nerve. Observations have been made chiefly on the changes in the myelin sheath of this nerve, using a modification of the Marchi method. The difficulties encountered in the use of this method or similar methods employing osmic acid are well known.

The cochlear nerve differs from other cranial nerves, with the exception of the optic, in that it is extremely susceptible to the action of various agents, such as drugs, alcohols and so forth. Recently Seiferth[2] has dissented from the opinion that degeneration of the auditory nerve may be due to the quinine and believes the results of its action can be attributed to effects upon the endothelial lining of the small vessels. Wittmaack[3] has recently confirmed and extended his studies of an earlier date on the action of quinine. He[4] has also concluded, from a study in which the auditory nerve was severed, that the laws of Wallerian degeneration do not apply to this nerve in the sense that they apply to a dorsal root ganglion and its nerve after the latter has been sectioned and allowed to degenerate.

Evidence of degeneration of the myelin sheath of the cochlear nerve by the Marchi method is not an unusual finding for normal

*From the George Williams Hooper Foundation, University of California, San Francisco, California.

Supported by a grant from the John C. and Edward Coleman Memorial Fund.

animals. Improper penetration of fixatives has been frequently blamed for the occurrence of these and other apparently pathological changes within the cochlea. After overcoming possibilities of artefacts due to fixation an attempt has been made to ascertain the reasons for changes of this nature within the nerves of normal animals. After examining sections of the temporal bones of animals of different species and ages, the effects of a variety of agents on the cochlear nerve were studied in order to ascertain the extent and nature of demyelinization changes. While the results presented deal only with this type of alteration, further studies, for which material is already available, will be concerned with the axis cylinders and nerve endings. In addition studies are in progress in which attempts are being made to link certain of the histopathological changes with functional tests for hearing in animals. The method available is that of Wever and Bray by which the cochlear response and the auditory nerve action potentials may be elicited.

TECHNIQUE

To obtain consistent and sufficiently controlled results the same procedure, with only the few exceptions noted, was followed for all animals used for these studies. Each animal was given an overdose of sodium barbital or dial "ciba" and urethane intraperitoneally. Ether and chloroform were avoided as anesthetics. The thorax of each animal was opened and a cannula tied in the aorta or left ventricle. The blood was washed out with a warmed solution of 5% magnesium sulphate in 2.5% potassium dichromate until the whole head of the animal was intensely stained. The length of time for this procedure was about eight minutes. Depending upon the size of the animal, 150 to 300 cc. of the perfusing fluid was used. Ten per cent formalin then replaced the fluid and after suitable fixation the head was removed and the temporal bones dissected. The right temporal bone of each animal was placed in a mixture of 5% magnesium sulphate in 2.5% potassium dichromate (80 parts) and formalin (20 parts) for 24 hours. It was then transferred to 10% formalin and allowed to remain for 48 hours. After this the bone was put into a mixture of the following: One per cent potassium chlorate (60 parts), 1% osmic acid (20 parts), formaldehyde (12 parts) and glacial acetic acid (one part). This method is a slight modification of the chlorate-osmic-formalin method described by Swank and Davenport[5]. It was found that either the use of physiological saline to wash out the blood for perfusion with formalin or ether anesthesia produced numerous fine blackened droplets in the nerve tissue.

The bone was allowed to remain in the chlorate-osmic-formalin mixture for a period of seven to ten days. This was sufficient time

to blacken the degenerating myelin. The cochleae of the rats usually required no decalcification following this length of time in the mixture. The temporal bones of the guinea pigs required 24 to 72 hours in 3% nitric acid for decalcification. Considerably longer time was required for the decalcification of temporal bones of kittens. After this procedure the material was washed for 24 hours in running water and prepared for imbedding either in celloidin or paraffin. The latter imbedding medium was found to be satisfactory for the rat ears. Sections of either paraffin or celloidin material were made at 10 micra in thickness and mounted in series of every tenth section. Cresyl violet served as a counterstain when desired.

EXPERIMENTAL

The studies have been made upon the following groups of animals: Twelve guinea pigs, ranging in weight from 150 to 260 gms., received daily injections (200 mgs. per kg. of body weight) of quinine bisulphate in a 2.5% solution. Four were killed after 43 days, four after 57 days and the same number after 71 days. Twelve guinea pigs, ranging in weight from 240 to 340 gms., received sodium salicylate in a 2.5% solution (200 mgs. per kg. of body weight) daily; six were killed after 49 days and six received injections for 63 days. The animals of each group were weighed periodically and the dosages adjusted on the basis of body weight.

A group of 12 kittens of three to five months of age were used for a study of the effects of a staphylococcus toxin* on the auditory nerve; four of these served as controls and received no injections. Eight received intraperitoneal injections of the toxin or in a few instances it was administered by stomach tube. Of this latter group six received single doses of the toxin sufficient in amount to produce marked symptoms (vomiting, diarrhea, etc.), but not lethal in effect. Of this same group two were killed the day following the administration of the toxin and four were allowed to live for 10 days. Two of the eight kittens received two additional doses at 14 day intervals and were killed 41 days after the initial dose.

Twelve rats (obtained from the Department of Biochemistry, University of California), representing two litters, were available for a study of the effects of vitamin A deficiency on the auditory nerve. These animals at the age of four weeks had been placed on a diet deficient in vitamin A. They were maintained on this diet for a period of 52 days. When manifestations of the deficiency became acute the animals were killed.

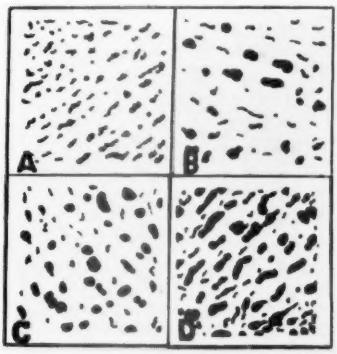
*A filtrate of starch broth or Dollman's medium in which organisms (staphylococcus aureus) isolated from bakery pies and cakes had been cultured.

Five rats (obtained from the laboratories of the Southern Pacific Hospital) whose diets had been deficient in vitamin B_1 were killed 36 days after being placed on the special diet. At this time they exhibited the characteristic signs and symptoms of vitamin B_1 deficiency. Seven rats obtained from the same source had received a diet deficient in vitamin B_2; three of these were killed after 50 days and four after 69 days. The latter group exhibited the most marked manifestations of this deficiency.

Twelve rats (obtained from the Institute of Experimental Biology, University of California) maintained for four weeks on diets deficient in vitamin B_6, were killed at the time the dermatitis and other signs of the deficiency became pronounced. Six rats (obtained from the Laboratory of Lepkowsky, Department of Poultry Husbandry, University of California) were also made available for study. These animals had received a vitamin B_6 deficient diet for three and one-half weeks and after this period they were given the missing factor in their food. In three weeks' time they appeared to have recovered from the dietary deficiency and were killed.

Since the "filtrate factor" (Jukes)[6] is an important vitamin of the B complex, similar technical procedures were carried out on chickens whose diets had been deficient in this vitamin. Fourteen birds were decapitated and the part of the head containing the organ of hearing was dissected free of muscles and immersed in the same fixatives as utilized for the other studies. Five of the birds had been maintained on the "filtrate factor" deficient diet for 26 to 33 days which was begun eight to nine days after hatching, while nine chickens were started on the diet eight to ten days after hatching. In the latter group the missing factor was supplied in their food after 21 to 24 days of the deficiency. Six of these remained on a normal diet for 12 days and were then killed, while three were kept for two months when all signs of the deficiency had disappeared. Nine chickens corresponding to the ages as the above received a normal diet and were used for control studies.

Thirty-four rats in various stages of vitamin D deficiency were obtained from O. Lang, Hooper Foundation, University of California. At the time these animals were started on a vitamin D deficient diet they weighed 50 to 60 gms. each. They were allowed to continue on the deficient diet for 18 to 23 days. Evidence of the deficiency was noted in each instance by means of the x-ray for the changes in the epiphyses of the long bones. As soon as the changes became pronounced they were given either cod or tuna fish oil for eight days with an additional two days allowed for assimilation of the oil. They



1

Fig. 1. Camera lucida tracings of degenerated myelin sheath for cochlear nerve in modiolus opposite the second turn of the cochlea. *A*, *B* and *C* represent the extent of degeneration found for the control group of three older guinea pigs and the most severe encountered in any controls. *D* shows the extent of the degeneration in a similar location for a guinea pig which received quinine subcutaneously for 57 days.

were then killed and the extent of repair in the epiphysis of the left femur was determined. For 20 rats of this group the healing effects of the oil administered represented a three to four plus cure, for seven rats there was a one to two plus cure and the remaining seven showed no improvement in the lesions. It was not possible to perfuse these animals with a fixative at the time they were killed, hence the results obtained were determined from sections of the cochleae of the temporal bones removed immediately after death of the animals by chloroform.

RESULTS

Of the 12 animals which received daily subcutaneous injections of quinine four were killed after 43 days. Moderate pathological changes were found in the basal whorls of the cochleae with only slight alterations near the middle and none in the apical turns. The nature of the changes was of the type previously described. In addition, changes in the myelin sheath as evidenced by use of the chlorate-osmic-formalin method were studied. Four of the guinea pigs were killed after 57 days of quinine injections. Sections of the cochleae of these animals revealed severe alterations which decreased in intensity

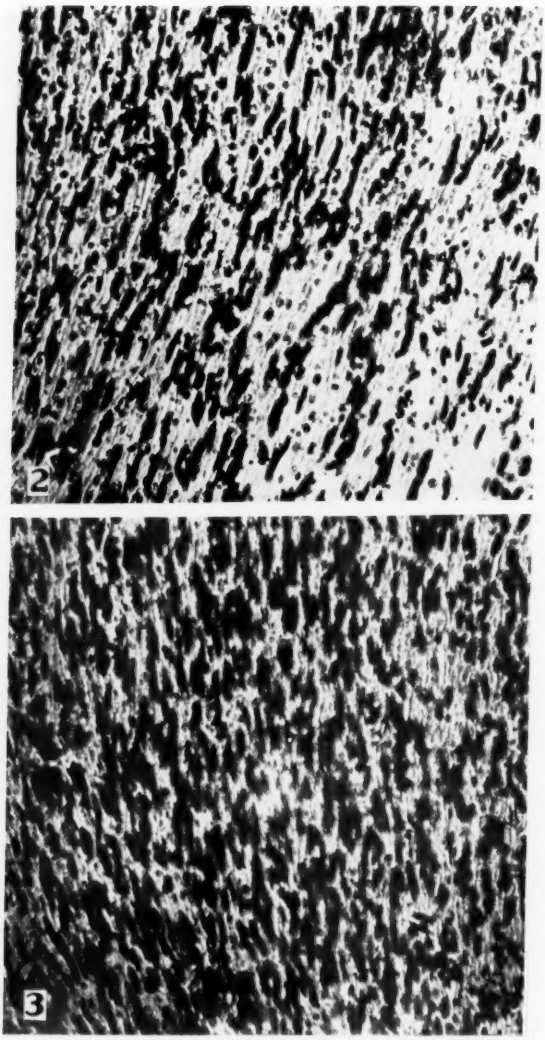


Fig. 2. Degenerating myelin sheath of nerve in modiolus, opposite second turn. From guinea pig which received quinine injections for 57 days Chlorate-osmic-formalin method. X500.

Fig. 3. Degenerating myelin in location similar to that of Fig. 2. From guinea pig which received quinine injections for 73 days. Chlorate-osmic-formalin method. X500.

from base to apex. Four animals which survived injections of the drug for 71 days revealed changes throughout the cochlea, but again these were more pronounced in the middle and basal whorls.

A comparison of the degenerated changes in the myelin sheaths of the nerve as it passed through the lamina spiralis ossea and distal to the spiral ganglion cells was made for the different whorls. An abundance of degenerating myelin in these areas appeared in the basal turns for the first group of animals (43 days). After 71 days the corresponding locations in sections of the cochleae of these animals showed evidence of degeneration of the sheath throughout. There was very little, if any, variation in the relative amount to be observed for the different regions. Changes in the myelin sheath in the region of the modiolus and opposite the second turn of the cochlea are illustrated in Figures 1d and 2. This animal had received the drug over a period of 57 days. There is considerably more degenerated myelin in the nerve for the corresponding location of an animal which received quinine for 71 days (Fig. 3).

Of the group of 12 animals which received sodium salicylate the six killed after 49 days revealed changes in the cochleae comparable to the 43 day group of quinine guinea pigs. Similarly there was a corresponding extent of pathological lesions between the guinea pigs which received salicylate for 63 days and those which received quinine for 71 days. In Figure 4 is illustrated the shrunken appearance of the ganglion cells and the demyelinization changes in the nerve distal to the ganglion cells. This photomicrograph represents the second whorl of the cochlea of one of the 63 day sodium salicylate animals. The progressive changes from base to apex of the cochlea were the same for these animals as was manifested in the group which received quinine over varying periods of time. The extent of changes in the myelin sheath of one of the cochleae is shown in Figure 5. The location is opposite the middle turn of the cochlea from a guinea pig of the 63 day group.

Sections of the cochleae of 16 control guinea pigs were not without evidence of myelin sheath changes. Of this group some were selected from the same stock as those given drug injections while a few were older animals. Four of the older animals, one to two years of age, weighed from 550 to 800 grams. Evidence of degeneration in the myelin sheath was marked and resembled in many ways the type and extent of degeneration found in the quinine and salicylate treated animals.

Figures 1a, b, c, represent the amount of myelin sheath degeneration in the modiolus opposite the second turn of the cochlea for

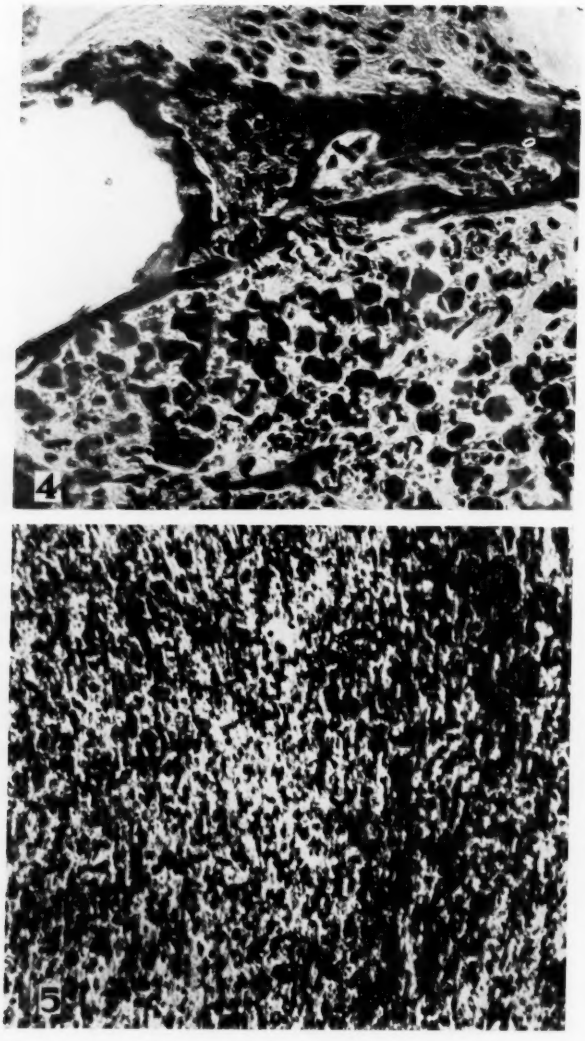


Fig. 4. Illustrates condition of spiral ganglion cells and degenerating myelin of nerve fibers in second whorl of cochlea for guinea pig which received sodium salicylate for 63 days. Chlorate-osmic-formalin method. X350.

Fig. 5. Degeneration of myelin sheath in modiolus opposite second turn of cochlea. From same section so illustrated in Fig. 4. Chlorate-osmic-formalin method. X350.

each of three older animals. For comparison the amount of degeneration at a similar location but for one of the guinea pigs which had received quinine for 57 days is shown in the lower right hand corner of the same figure. These outlines made by means of the camera lucida of the varying degrees of degeneration in the myelin sheath serve to illustrate the differences under consideration.

Twelve of these control animals were of the same age and stock as the experimental animals and weighed from 150 to 450 gms. Of these, eight revealed slight to moderate demyelinization changes in the cochlear branch of the nerve. There was, however, a considerable difference when compared with the sections of cochleae from animals which had been injected with the drugs. Of the guinea pigs of this control group, four revealed no changes in the myelin sheath. It was obvious that drugs acting directly or indirectly contribute to changes of the nature described.

STAPHYLOCOCCUS TOXIN

Of the eight kittens which received sublethal doses of staphylococcus toxin only two revealed extensive degenerative changes in the myelin sheath of the cochlear nerve. These two animals received the toxin in three doses at 14 day intervals and while the changes were more pronounced for the middle and basal whorls of the cochlea there was also apparent demyelinization in the apical turns as well. The changes in the nerve of these kittens which were killed the day following the injection of a sublethal dose were similar to the findings of a control group of four kittens. The latter received no toxin. The four animals which survived for 10 days on an initial dose exhibited less pronounced changes than the two killed after repeated doses but which were allowed to live for 41 days.

The spiral ganglion cells in the middle and basal whorls of the cochlea were obviously damaged by the toxin. They were shrunken and homogeneously stained. Such findings were in contrast to the appearance of the sipiral ganglion cells in the apical turns of the same cochlea which appeared to be undamaged. The latter resembled the findings of the ganglion cells for the entire cochlea of the control animals.

AVITAMINOSES

Degenerating myelin was encountered in sections of the cochleae for many of the different groups of animals on various vitamin deficient diets. The results and summary of the experimental procedure for each group are given in Table I.

TABLE I.

DEMYELINIZATION OF THE COCHLEAR NERVE FOR VARIOUS VITAMIN DEFICIENT ANIMALS

Vitamin Deficiency	Number of Animals	Length of Time on Diet	Missing Factor Added to Diet	Changes in Myelin Sheath For Different Turns of Cochlea			Myelin Sheath Changes in Other Nerves
				Basal	Middle	Apical	
A	12	52 days	.....	Moderate	Slight	Slight	Few fibers in vestibular nerve.
B_1	5	36 days	.....	Moderate	Slight	None	Few fibers in vestibular nerve.
B_2	3	50 days	.....	Moderate	Slight	Slight	Few fibers in vestibular nerve.
	4	69 days	.....	Moderate	Slight	Slight	Few fibers of vestibular, 5th and 7th cranial and sciatic nerves.
B_6	12	28 days	.....	Severe	Moderate	Slight	
	6	24 days	21 days	Slight	Slight	None	Few fibers in vestibular nerve.
D	20	18-23 days	8 days	Moderate	Slight	Slight	Few fibers in vestibular nerve.
	7	18-23 days	8 days	Moderate	Moderate	Slight	Few fibers in vestibular nerve.
	7	18-23 days	8 days	Severe	Moderate	Moderate	Few fibers in vestibular, 5th and 7th cranial and sciatic nerves.
"Filtrate factor"	5	26-33 days	.....	Moderate amount of demyelinization			None in vestibular nerve.
	6	21-24 days	12 days	Moderate amount of demyelinization for 4. Only slight changes for 2.			Slight changes in vestibular nerve for 3.
	7	21-24 days	61 days	Slight changes, similar to control group.			Very few changes in vestibular nerve.

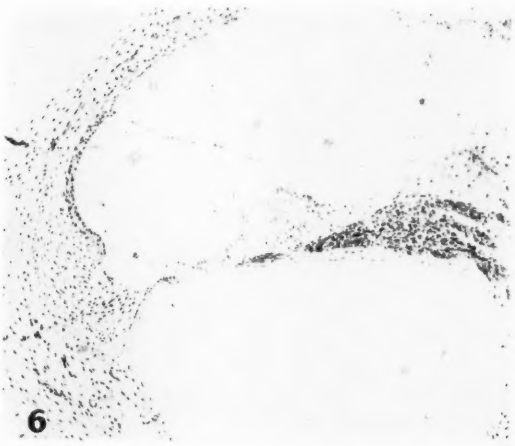


Fig. 6. Section through cochlear duct and scalae of one of the basal turns of a vitamin B_6 deficient rat. Chlorate-osmic formalin method and cresyl violet. X150.

Vitamin A deficient rats (52 days) revealed moderate changes in the myelin sheath of nerve fibers in the basal turns. Only slight evidence of change was found in the middle and apical turns.

Of five animals whose diets were deficient in vitamin B_1 for 36 days few alterations, similar in nature to those of vitamin A deficient animals, were revealed. A few fibers of the fifth and seventh cranial and sciatic nerves of these animals showed demyelinization changes. Vitamin B_2 deficient animals, of which there were seven, showed for three rats fewer changes than for the remaining four. The latter had been maintained on a diet deficient in vitamin B_2 for a longer period of time. Sections of the cochlear nerve for vitamin B_6 deficient rats showed marked changes after 28 days on the diet. There was an occasional degenerated fiber in the fifth and seventh cranial nerves and a few such fibers in the sciatic nerves of these animals. A smaller group of six animals which had been on the vitamin B_6 deficient diet for 24 days and were then given the missing factor in their food for a period of 21 days revealed fewer changes. There was a tendency for the sheath cells to proliferate, particularly in the extreme distal portion of the myelinated part of the nerve. The apical turns of the cochlea showed only slight changes. Figure 6 is a lower power

view of the second whorl of the cochlea of one of the vitamin B_6 deficient animals. The degree of the degeneration in the nerve is greatest at the point where the myelin sheath first appears. This is illustrated at a higher power in Figure 7, which is from the same area as the lower power photomicrograph. Figure 8 shows the extent of changes in the nerve just distal to the spiral ganglion cells. The nerve fibers within the lower half of the modiolus are illustrated in Figure 9.

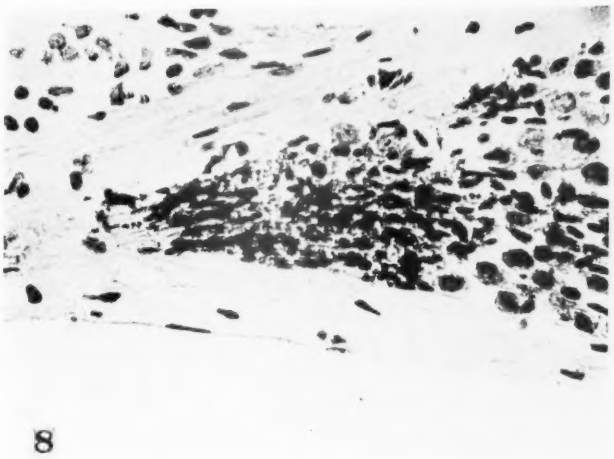
The cochlear nerves of rats, the diets of which were deficient in vitamin D for a period of 18 to 23 days, revealed changes corresponding to the degree of the deficiency. Twenty rats in which the epiphyseal lesions had practically healed after the administration of cod or tuna fish oils showed less degenerating myelin than the groups in which the healing had not taken place or was considerably less. Had a period longer than 10 days been allowed for recovery to take place in these animals it is probable that even fewer changes might have been encountered.

The "filtrate factor" deficient chickens revealed demyelinization changes in the nerve to the organ of hearing. The vestibular nerve showed few, and in many instances no changes. The findings corresponded to the length of time the animals were maintained on the deficient diet. The group of birds in which the evidence of deficiency had been satisfactorily produced after 21 to 24 days and which were then given the missing factor in their diets for 12 days showed only slight differences from those maintained on a deficient diet for the same length of time. The three birds which received a normal diet for 61 days following the production of typical characteristics of a "filtrate factor" deficiency showed considerably less demyelinization. The control group of nine birds while not entirely free from evidence of such changes revealed much less extensive degenerative changes in the myelin sheath.

COMMENT

The not uncommon finding of a degenerated myelin sheath of the cochlear nerve in many laboratory animals has led to a more or less universal acceptance of the fact that such may occur without apparent cause. It may be possible that the physico-chemical composition of the myelin sheath of this particular nerve varies from that of other nerves. It is apparently influenced by many factors, including age. One is aware of the fact that a neurokeratin network does not exist in nerve fibers (Hoerr[7]), and hence the ease with which the myelin becomes degenerated cannot be attributed to a faulty network within it. Similarly the possibility of improper fixation can

7



8

Fig. 7. Photomicrograph at higher power of Fig. 6 showing changes in nerve in most distal medullated part. X500.

Fig. 8. Degenerated myelin in fibers just distal to spiral ganglion cells. Same section as Fig. 6. X500.

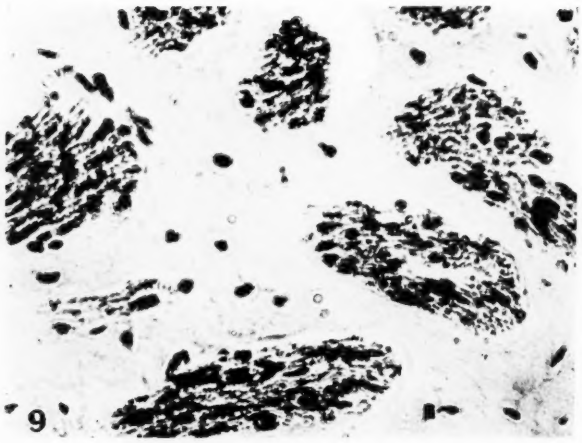


Fig. 9. Degenerated myelin in nerve within modiolus and opposite the region shown in Fig. 6. X500.

be disregarded in view of the recent advances made in technical procedures. An explanation for the occurrence of changes in the myelin sheath of control animals is to be found in those factors which result in demyelinization generally. Hirose[8] found that degenerative changes appeared earlier and were more marked in the cochlear nerve than in the vestibular nerve after severing the auditory nerve in animals. In the course of the present studies the vestibular nerve never revealed the same amount of demyelinization for drugs, toxin or missing dietary factors which appear to have produced it in the cochlear nerve. This relative instability may be finally explained by the fact that phylogenetically the cochlear nerve is younger.

Various substances may act differently upon the nerve to produce changes of this nature, and it is probable that only with the degeneration of the axis cylinders that function becomes appreciably impaired. Certain substances may act directly to produce changes similar to those observed by Speidel[9] for alcohol on the nerves in the tail of the tadpole. Others may act indirectly through the vascular supply as probably quinine, salicylates and toxins do. Neurotoxins may destroy the ganglion cells with subsequent changes in the myelin sheath. It would seem that the vitamin deficiences which are known to be associated with certain nervous system manifestations may pro-

duce changes in the myelin sheath by liberation of an enzyme. The latter is, however, only a hypothetical explanation which awaits experimental proof.

A survey of the group of vitamin deficient animals reveals changes in the nerve for the lack of vitamins A, B_1, B_6, the "filtrate factor" and D. In other words, each of the vitamin deficiencies studied showed some degree of myelin degeneration for the cochlear nerve which was significant in its variation from the findings for the animals maintained on normal and adequate diets. Furthermore, animals on recovery diets but previously depleted for vitamin B_1, "filtrate factor" or vitamin D showed sufficient regeneration within the nerve to warrant the association of the lack of either of these dietary factors with pathological findings. Adequate material for a study of regeneration by the other nutritional factors was not available at the time this study was in progress. It is probable that similar findings might have been encountered.

To attempt a comparison between the different vitamin deficiencies and peripheral nerve pathology in the light of our present knowledge would be futile. A review of the literature on the subject results only in confusion. Wolbach[10] believes the effects of starvation on the maintenance of the myelin sheath should be determined before the effects of certain of these deficiencies are correlated with changes in it. Recently Eveleth and Biester[11] have reported the occurrence of severe myelin degeneration in peripheral nerves of dogs fed on rations including vitamins A, B complex, D and E. They were unable to correlate signs of incoordination in a disease of swine with the appearance of the myelin sheath and concluded that different etiological agents may cause each. On the other hand there may be a factor common to many of the vitamin deficiencies which is responsible for changes in the myelin sheath. Particularly does this seem to be true in the cochlear nerve.

If hearing impairment is to be associated with nutritional disturbances as Selfridge[12] contends then one might expect nerve deafness to be an end result, if not an accompanying symptom, for certain clinical cases of beri-beri, pellagra, rickets and so forth. The literature is practically devoid of any mention of nerve deafness in relation to a particular vitamin-lack. An experimental study of the avitaminoses may or may not produce results directly applicable to humans, but it is doubtful that a subclinical dietary deficiency would result in profound changes within the auditory mechanism. It seems possible that an already existing nerve deafness may be alleviated to some

extent by the use of certain vitamin concentrates. Whether this may be due to general metabolic factors or to specific action on the cochlear nerve will require a wealth of clinical and experimental evidence to determine.

Degeneration of the myelin sheath of the cochlear nerve is not by itself an adequate criterion for judging the effects of any agent which might produce nerve deafness. It is a factor to be considered in its pathology in conjunction with other changes in the nerve, the end-organ, the stria vascularis and spiral ganglion cells. The extent of these alterations and their nature remains to be correlated with hearing tests before the rôle which histopathological changes of this nature might play in influencing hearing can be determined. It is our hope to continue our work along these lines.

SUMMARY AND CONCLUSIONS

The myelin sheath of the cochlear nerve is relatively unstable and the action of a variety of agents may result in the production of degenerative changes in this sheath. Factors such as age of the animal tend to increase the occurrence of degenerating myelin in control animals. In other words, each of the vitamin deficiencies studied showed some degree of myelin degeneration for the cochlear nerve which was significant in its variation from the findings for the animals maintained on normal and adequate diets.

Experimentally the changes are more pronounced in the nerve within the basal whorls of the cochlea and peripherally. Demyelinization gradually extends towards the middle and apical turns and finally involves the nerve fibers within the modiolus. The process thus extends from the periphery towards the more central pathways as has been shown by changes in the auditory nerve with its fibers from the cochlea and vestibule.

Animals which received quinine and salicylate for six to ten weeks showed extensive degenerative changes. A staphylococcus toxin administered to kittens in several injections and over a period of several weeks resulted in drastic changes within the myelin sheath. Various vitamin deficient animals including avitaminoses A, B_1, B_2, B_6, "filtrate factor" and D showed varying grades of changes within the myelin sheath which could be correlated with the severity of symptoms produced and the length of time the animals received deficient diets. Evidence tends to point towards a factor common to the different avitaminoses and which is capable of producing myelin sheath changes in the cochlear nerve.

BIBLIOGRAPHY

1. Covell, W. P.: A Cytologic Study of the Effects of Drugs on the Cochlea. Arch. Otolaryng., 23:633-641, 1936.

2. Seiferth, L. B.: Über die Wirkung des Chinins auf das Gehörorgan und den Vestibular Apparat, zugleich ein Beitrag zum experimentellen Lagenystagmus. Ztschr. f. Hals, Nasen- u. Ohren., 37:367-388, 1935.

3. Wittmaack, K.: Über Chinin Workung im Gehörorgan. Ztschr. f. Hals-Nasen- u. Ohrenh., 39:211-222, 1936.

4. Wittmaack, K.: Über sekundare Degeneration im Cochlearnerven und über die funktionelle und biologische Beziehung zwischen Cortischem Organ und Hörnerven. Acta Oto-laryngologica, 23:274-289, 1935.

5. Swank, R. L. and Davenport, H. A.: Marchi's Staining Method. Studies of Some of the Underlying Mechanisms Involved. Stain Technol., 9:11-19, 1935.

6. Jukes, T. H.: Further Observations on the Assay, Distribution and Properties of the Filtrate Factor. J. Biol. Chem., 117:11-20, 1937.

7. Hoerr, N. L.: Cytological Studies by the Altman-Gersh Freezing-Drying Method. IV. The Structure of the Myelin Sheath of Nerve Fibers. Anat. Rec., 66:91-95, 1936.

8. Hirose, T.: Histo-pathologische Studien über das innere Ohr nach Acusticus-stammdurchschneidung. Tr. Soc. path. jap., 23:939-941, 1933.

9. Speidel, C. C.: Studies on Living Nerves. V. Alcoholic Neuritis and Recovery. J. Comp. Neur., 64:77-113, 1936.

10. Wolbach, S. B.: The Pathologic Changes Resulting from Vitamin Deficiency. J. A. M. A., 108:7-13, 1937.

11. Eveleth, D. F. and Biester, H. E.: The Significance of Myelin Sheath Degeneration and Its Relation to Incoordination. Am. J. Path., 13 257-266, 1937.

12. Selfridge, G.: Can Certain Diseases of the Ear, Nose and Throat, Especially Degeneration of the Eighth Nerve, be Classified as "Deficiency Diseases"? Laryngoscope, 46:85-106, 1936.

LXXVI

SHEATH OF THE INTERNAL CAROTID ARTERY: A ROUTE FOR INFECTIONS FROM PRIMARY LESIONS*

IRA FRANK, M.D.

AND

CELIA SCHEER, M.D.

CHICAGO

The purpose of this investigation was to trace the route of intracranial complications originating from pharyngeal infections. Though such a complication is not very common, we had the opportunity to study two relevant instances where an acute meningitis followed a severe tonsillar infection. A neck dissection in these two instances revealed that the inflammation apparently had spread into the meninges by way of the sheaths of the internal carotid arteries.

In the following a review of the pertinent literature is given and an attempt is made to explain the routes of the propagation of the infection via the carotid sheath on an anatomic-embryologic basis. Finally, the results of a number of experiments are given which have been conducted to reproduce the intracranial complications in dogs.

LITERATURE

In reviewing the literature it was of interest to note that so far no experimental studies in animals have been carried out to explain the pathogenesis of endocranial complications in buccopharyngeal infections. The lack of interest in this problem is most likely due to the general belief of the extreme rarity of this complication universally shared by authors of voluminous textbooks, as well as by those reporting individual cases. In the entire international literature only two reports (Wessely,[1, 2, 3] Ameriso[4]) were encountered dealing with a thorough study of this problem. Both authors discussed carefully the routes of infections based on anatomic-pathologic and experi-

*From the Department of Pathology of the Nelson Morris Institute of the Michael Reese Hospital and the Department of Laryngology of the Michael Reese Hospital.

mential studies. They also reviewed the literature. The combined efforts of both authors yielded a collection of 26 cases (including their own case studies). The opinion is thus prevalent throughout the literature that this complication is an extreme rarity. The frequency of upper respiratory infections and the relative rarity of the reported complications at first glance seem to justify this opinion. However a more systematic and careful perusal of the world's literature revealed to us a total of 87 cases since the first case reported in 1865. All types of endocranial complications were included; the primary focus being located in the tonsils, the paratonsillar tissues, the pharynx, the nasopharynx, the retropharyngeal, parapharyngeal spaces and the parotid loge; in other words, all the structures which are anatomically related to the sheath of the internal carotid artery. In the accompanying table I the pertinent features of the reported cases are listed. In the following these cases will be summarized in short.

Age.—In only 72 instances the age was stated. Eight patients were between 2 and 10 years of age; 13 between 10 and 20; 32 between 20 and 40; 18 between 40 and 61 and one was 81 years old. It seems that endocranial complications of bucco-pharyngeal infections occur more frequently in adults than in children, the highest incidence being between the ages of 20 and 61. Although meningitis and upper respiratory infections are more common in children than in adults, one is impressed by the facts that bucco-pharyngeal infections may become more dangerous in adults than in children and that the foci of infection in meningitis and sinus thrombosis apparently may be different in childhood than in adult life.

Sex.—The sex was mentioned in only 54 patients out of 87. There were 39 males and 15 females.

The Primary Focus.—The incidence of involvement of the different structures in the mouth and the neck and the different types of inflammation was as follows: There were 23 instances of suppurative inflammation of the tonsillar and paratonsillar tissues; 17 cases presented an inflammation of the tonsils and of the adjacent portions of the pharynx, the retropharyngeal and parapharyngeal spaces. In some of these the inflammation had spread unlimited throughout all the tissues of the neck. In 17 instances an acute non-suppurative tonsillitis was present. A few of these also revealed a chronic inflammation. Of 80 cases there were only six of uncomplicated tonsillectomy and nine tonsillectomies complicated by abscess formation in the paratonsillar tissues and the tissues of the neck. In nine instances a cervical abscess was found. Two patients had an acute inflam-

mation of the pharynx. In two other instances there was an abscess in the pterygo-maxillary fossa. In one of these patients an otitis media and a retropharyngeal abscess were also found. In two cases an abscess in the parotid gland was encountered, one of which originated from an alveolar abscess.

It is thus apparent that endocranial complications occur in the majority of cases of severe inflammations of the tonsillar and paratonsillar areas (51 patients).

Endocranial Complications.—All the structures within the skull as well as the bony walls themselves may become involved in instances of bucco-pharyngeal infections. Roughly six different groups may be distinguished. There were 19 instances of meningitis, of which 14 were proved at post mortem examination. There were 16 instances of thrombosis of the cavernous sinus, of which nine were discovered at autopsy. Thirty-one cases revealed meningitis and thrombosis of the cavernous sinus. A brain abscess was found twelve times and was in nine cases complicated by a localized meningitis.

Microscopic studies.—Microscopic examinations were reported in only a few cases. Wessely[2] examined very carefully and thoroughly one case by means of topographical-serial sections. He was able to demonstrate the spread of the infection from the tonsil into the parapharyngeal space and from there through the foramen ovale and spinosum to the middle fossa of the skull. These findings formed the basis for his experimental-anatomical studies and his explanation of the pathogenesis of intracranial complications to which we shall refer later. In another case he described autolysis of the sheaths of the vessels in the neck. Shapiro[5] and Vogel[6] in the presentation of their cases described an inflammation of the sheaths of the carotid artery without, however, definitely localizing its position in the sheath. Lewin[7] reported in his case the presence of granulation tissue in the right cavernous sinus and an inflammation of tissues surrounding the internal carotid artery. Schlittler[8] found a suppurative inflammation of the carotid plexus. Ameriso[4] described an extensive involvement of the walls of the internal carotid artery in its cavernous portion which, however, may have been secondary to the suppurative process in the sinus itself.

The Pathways of Infection.—The spread of infection from the buccopharyngeal region to the endocranium as described in the literature is by venous channels, by direct extension of a phlegmonous inflammation from the parapharyngeal space, by erosion of the bone, and by way of the lymphatics.

Venous Channels.—The first studies on these pathways were made in France. Panas[9] (1885) and his school considered the venous channels the route of spread. The infection supposedly spreads from the tonsillar veins to the pharyngeal plexus entering the skull through the vein of the foramen ovale which communicates directly with the cavernous sinus. Festal[10] (1887) in an anatomic study demonstrated the existence of such a vein in the foramen ovale. Terson[11] (1893) was able to find in one of his cases a thrombophlebitis of this vein and likewise the direct communication with the pharyngeal plexus and the cavernous sinus. Dietrich[12] in an extensive summary on this subject referred only to the type advocated by Terson. Ameriso[4] in 1935 after a careful study of the venous pathways in instances of cavernous sinus thrombosis following tonsillar infections suggested three ways of spread: 1. From the tonsils to the inferior palatine vein, to the pterygoid plexus, to the vein of the foramen ovale, and to the cavernous sinus. 2. From the tonsil to the tonsillar plexus, to the pterygoid plexus, to the facial vein, to the ophthalmic vein, to the inferior ophthalmic vein, to the superior ophthalmic vein, and to the cavernous sinus. 3. From the tonsil to the tonsillar plexus, and then directly to the internal jugular vein, to the bulb of the internal jugular vein, to the inferior petrosal sinus, and to the cavernous sinus.

Direct Extension.—Wessely[3] in 1932 added a new conception of the spread of infections from the tonsil to the endocranium based on a thorough microscopic examination of one of his cases. In cases of phlegmonous inflammation of the tonsillar region the spread supposedly occurs through the parapharyngeal space upwards to the base of the skull and into the brain along the sheaths of the vessels and nerves located in the foramen ovale, lacerum and spinosum. Wessely[1] attempted to prove this mode of spread in human cadavers by injections of india ink into the paratonsillar tissues under moderate pressure. He was able to demonstrate the presence of ink in all cases in the parapharyngeal space and at the base of the skull. He admitted, however, instances in which an inflammation spreads also by venous channels alone or by venous channels through the parapharyngeal space.

Erosion of the Bones.—There are only a few cases reported in which this mode of spread may be assumed. These cases revealed an osteomyelitis of the bones of the base of the skull (Silverberg,[13] Wylie[14]).

Lymphatic Spread.—Several authors have expressed the opinion that the infection may spread along the sheaths of the vessels (Macewen[15]) assuming the presence of lymph channels. Ferretti,[16]

reporting a case of a brain abscess following tonsillitis, considered that the ascending lymphatics may convey the infection to the brain substance since the lymphatics of the brain open into the deep lymph nodes of the neck. Infection of these lymph nodes of the neck draining the tonsillar area may by retrograde-spread involve the brain. Studies by Turner and Reynolds[17] of the possible spread of infections from the nasal and naso-pharyngeal cavities by way of lymphatic channels, however, failed to confirm this possibility.

It can easily be seen from this review of the literature that there are various routes by means of which a pharyngeal infection may spread into the cranial cavity. None, however, could be reproduced in experimental animals. As was mentioned before our interest was aroused as a result of post mortem findings in two cases in which the sheath of the internal carotid artery showed evidence of acute inflammatory changes starting from the pharyngeal portion of these arteries and extending up to its cavernous portion. Thus the internal carotid artery and particularly its sheath seemed significant as a pathway in the causation of the intracranial complications. It was therefore thought wise to review the pertinent anatomical and embryological relationship of the internal carotid arteries and their sheaths.

The sheath of the internal carotid artery.—In 1913 Ferron[18] demonstrated the continuation of the sheath of the internal carotid artery into the petrous and cavernous portions. The sheath constitutes the deep layer of the wall of the cavernous sinus, while the superficial layer is formed by the dura mater.

This anatomic fact may be of great importance in the pathogenesis of basal meningitis following upper respiratory infection, and places our experimental study on a sound anatomic basis.

Of equal importance and significance is the relationship of the sheath to the organs in the neck. Rather numerous careful studies have been made in recent years by Testut,[19] and Hall.[20] Hall[20] discusses and exposes clearly in many illustrations this relationship. He found that the contents of the carotid sheath form a part of the parapharyngeal space, which is described in the literature under different names, such as the pharyngo-maxillary, the parapharyngeal and the lateral pharyngeal space. The parapharyngeal space is divided by the styloid process in two distinct compartments, the prestyloid or anterior parapharyngeal space, and the restrostyloid or posterior parapharyngeal space. The carotid sheath and its contents constitute the posterior parapharyngeal space. The carotid sheath

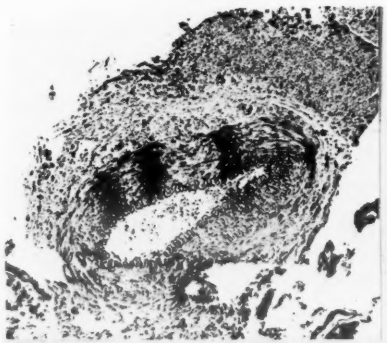


Fig. 1.

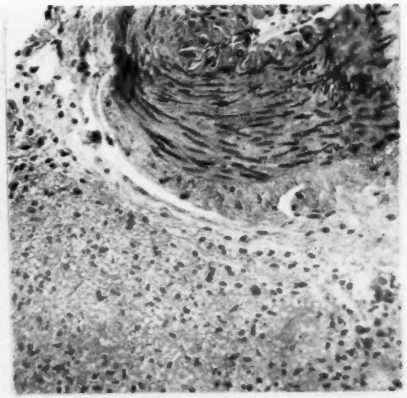


Fig. 2.

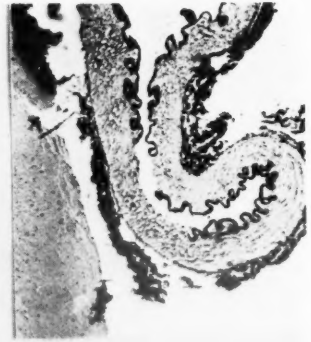


Fig. 3.

Fig. 1. Petrous portion of thei nternal carotid artery (dog). Note the acute inflammatory changes in the periarterial region. (Hematoxylin-eosin preparation; x 43.)

Fig. 2. Higher magnification of Figure 1. Note the inflammatory cells. x 154.

Fig. 3. Petrous portion of internal carotid artery (dog). Note dark stained areas (clumps of organisms) in periarterial region. (Gram-Weigert preparation; x 70.)

forms the border of the retropharyngeal space and communicates indirectly with the parotid loge through the anterior compartment of the parapharyngeal space. The tonsil and the paratonsillar spaces are separated from it only by the superior pharyngeal constrictor and its fascia, which, however, form a very incomplete barrier. This is evidenced by the frequent occurrences of parapharyngeal abscesses after tonsillar and paratonsillar suppurative inflammations. As soon as the artery enters the skull through the external carotid foramen, it is surrounded by the venous plexus, which follows the artery along its entire course in the bony canal. This canal is curved and passes obliquely from behind and lateralward, forward and medianward through the pyramid and merges near the apex by an irregular opening, the internal carotid foramen, partly on the inferior and partly on the anterior surface. Near the external carotid foramen can be seen in the carotid canal, the small openings of the canaliculi caroticotympanici through which passes the right carotico-tympanic artery (a branch of the internal carotid artery) which passes upward to the middle ear. The internal carotid artery with its sheath is separated from the tympanic cavity by a thin, bony lamella which in young subjects is cribriform and often partly absorbed in old age. Farther forward the artery is separated from the semilunar ganglion by a thin plate of bone which forms the floor of the fossa for the ganglion and the roof of the horizontal portion of the carotid. Frequently the bony plate is more or less deficient and then the ganglion is separated from the artery by a fibrous membrane.

The artery is separated from the bony wall of the carotid canal by a prolongation of the dura mater and is surrounded by a number of small veins and by filaments of the carotid plexus derived from the ascending branch of the supracervical ganglion of the sympathetic trunk.

The artery at first ascends to the posterior clinoid process, then passes forward by the side of the body of the sphenoid bone and again curves upward on the medial side of the anterior clinoid process and perforates the dura mater forming the roof of the sinus. This portion of the artery is surrounded by filaments of the sympathetic nerve, and on its lateral side is the abducent nerve.

Having perforated the dura mater on the medial side of the anterior clinoid process, the internal carotid passes between the optic and oculo-motor nerve in the anterior perforated substance at the medial extremity of the lateral cerebral fissure where it gives off its terminal or cerebral branches.

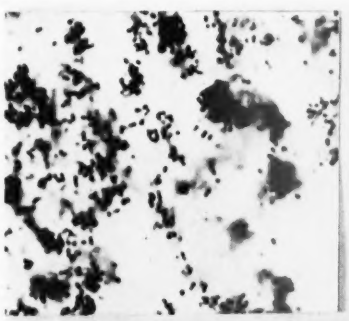


Fig. 4.

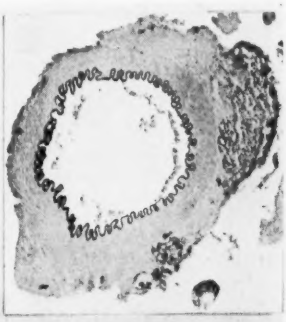


Fig. 5.

Fig. 4. Higher magnification of Figure 3. Note the abundance of cocci. (Gram-Weigert preparation; x 560.)

Fig. 5. Cavernous portion of internal carotid artery (dog). Note the clumps of organisms in the periarterial space. x 43.

MATERIAL AND METHODS

Experiments were carried out on dogs to see, first, whether or not a direct pathway could be demonstrated along the sheath of the internal carotid artery to the intracranial cavity and, secondly to see whether or not it might be possible to produce some intracranial complications observed in instances of tonsillar and pharyngeal infections by an injection of pathogenic microorganisms into the sheath of the internal carotid artery in dogs.

Twenty-four healthy adult dogs and nineteen puppies were used. Under nembutal anesthesia the bifurcation of the carotid artery was exposed and the internal carotid artery, which is a very small vessel in the dog, was dissected out over a distance of about 0.5 cms. in length. Injections by means of needles and syringe were given into the sheath of the internal carotid artery close to the bifurcation, the needle being directed cranially and pointing towards the upward course of the internal carotid artery. The material injected consisted of 24 to 48 hour broth cultures of various bacterial strains which were obtained from the subarachnoidal exudate in instances of meningitis and of cultures of hemolytic streptococci obtained from

the pharynx of a dog. Also india ink and gum tragacanth were used either alone or in conjunction with the bacteria.

An autopsy was performed on all dogs which either died spontaneously or were sacrificed after a certain lapse of time. The common carotid arteries, their bifurcations, and the cervical, petrous and cavernous portions of the internal carotid arteries were dissected, carefully inspected grossly and studied microscopically. The brain and the meninges were examined microscopically, sections being taken from various regions but especially from the base of the brain.

RESULTS

Tables II to IV summarize the results of the experiments. Table I shows that bacteria injected into the sheath of the internal carotid artery may produce an inflammation of the cervical portion of the sheath of the artery but the inflammation remains more or less localized. In three dogs the inflammation was also produced by the injection of streptococci and india ink. Table II makes it clear that injection of the organisms in addition to the injection of foreign bodies in a number of instances produce an inflammation of the sheath of the artery. In one instance india ink alone caused the inflammation. In a single dog meningo-encephalitis was found; the sheath of the cervical portion of the internal carotid artery in this dog also showed inflamamtory changes. The third table indicates that in puppies acute inflammatory changes occasionally could be produced in the cervical, petrous and also cavernous portions of the internal carotid artery. Also bacteria were occasionally encountered in these regions. It may be pointed out especially that bacteria were never found within the lumen of the internal carotid artery, nor were thrombi seen in this vessel.

DISCUSSION

Under various conditions, microörganisms, some of which were taken from the exudate in instances of meningitis in humans and some from dogs in instances of acute pharyngitis, were injected into the sheath of the internal carotid artery. Following the methods of Steinberg and Goldblatt,[21] who failed to kill the animals by injections of microörganisms into the peritoneal cavity but who were able to cause death by the injection of foreign bodies in addition to bacteria, india ink and gum tragacanth were introduced into the sheath of the internal carotid artery. In only a single instance meningo-encephalitis was obtained. This single finding, which could not be reproduced, may merely be stated but cannot be used for any significant conclusions.

While the experiments on adult dogs revealed the spread of the inflammation within the sheath of the cervical portion of the internal carotid artery, the experiments performed on puppies showed that the inflammation extended throughout the sheath of the petrous and also the cavernous portions. In two instances bacteria were also encountered in these regions and in one case thrombosis of the cavernous sinus was present. Unfortunately all of the puppies died a few days after the first or second injection. This may possibly account for the fact that an infection of meninges was not found since the animals died too soon. It is also possible that the resistance in dogs may be so high that the bacteria disappeared before they could ascend.

These experiments indicate that the sheath of the internal carotid artery may actually constitute a pathway for a spread of an infection from the region of the pharynx and tonsils, even though in our experiments the inflammatory changes of the sheath at a distance from the site of injection were encountered relatively rarely. It is interesting to note that these changes could be demonstrated only in puppies, who died shortly after the introduction of the microörganisms.

On the basis of these experiments it seems imperative to examine carefully the sheath of the cervical, petrous and cavernous portions of the internal carotid artery in all instances of intracranial complications from primary tonsillar infections for a demonstration of a possible pathway of the spread of the infection.

SUMMARY

A summary of the literature pertaining to reported cases of intracranial complications resulting from pharyngeal infections is given with special reference to the pathway of the infections. Eighty-seven such instances are quoted. Experiments on dogs were conducted to ascertain if a direct pathway could be demonstrated along the sheath of the internal carotid artery to the intracranial cavity and if intracranial complications could be produced by injection of pathogenic microörganisms into the sheath of the internal carotid artery. In two instances organisms were encountered in the sheath of the petrous and cavernous portions of the internal carotid artery after injection of these into the sheath of this artery at its origin from the common carotid.

104 South Michigan Ave.

TABLE I.

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
1.	v. Stein[22] 1894	32		Phlegmonous pharyngitis	Purulent leptomeningitis; left temporal lobe abscess	Sphenopalatine fossa, inferior orbital fissure, gasserian ganglion	None	Small abscess in left temporal muscle
2.	DeLapersonne[23] 1885	46	Male	Gangrenous phlegmonous tonsillitis	Basal purulent meningitis, pus in cavernous petrosal and circular sinuses	Tonsillar abscess, palatine veins, sphenopalatine veins, orbital veins, cavernous sinus	None	Pituitary body was surrounded by pus, sella turcica and the body of sphenoid eroded and friable
3.	Zawadski[24] 1886	46	Male	Mandibular angle and pharyngeal space filled with pus.	Basal purulent meningitis, purulent thrombosis in cavernous and petrosal sinuses	Not stated. The veins in the primary focus were thrombosed	None	
4.	Riese[25] 1900	52	Male	Abscess in lateral pharyngeal wall.	Purulent thrombosis of cavernous sinus.	Periosteum of maxillary bone, pterygoid fossa, pterygoid plexus, foramen ovale, cavernous sinus	None	Muscles in the pterygomaxillary fossa infiltrated with pus. Pathway also possible over meningeal vein direct to cavernous sinus
5.	Tollens[26] 1903	19	Female	Peritonsillar abscess and phlegmonous pharyngitis	Generalized purulent meningitis; purulent thrombus in cavernous sinus	Not stated by author	None	Phlegmon of neck. Thrombosis of ophthalmic veins. Optic nerve, antrum of Highmore showed no changes.

6. Davis[27] 1913	10		Unilateral parenchymatous tonsillitis	Cavernous sinus thrombosis	No autopsy	None	Author had two more cases of post-tonsillitic cavernous sinus thrombosis. One patient recovered, but was blind
7. Kandler 1907 quoted in Wessely[1]	35		Peritonsillar abscess, preauricular and retropharyngeal abscess	Purulent basilar meningitis. Abscess of temporal lobe	Not stated by author	None	
8. Proskauer[28] 1914	20	Male	Peritonsillar abscess following tooth extraction	Purulent hemorrhagic external and internal pachymeningitis and circumscribed leptomeningitis of temporal lobe	Not stated by author	None	Purulent phlebitis of internal jugular vein. Destruction of foramen ovale
9. Jacques and Lucien[29] 1908	46		Peritonsillar abscess. Phlegmon of right side of neck	Suppurative basilar meningitis; cortical encephelomalacia; thrombosis of cavernous and circular sinuses; pituitary softened	Not stated	None	Jugular vein free. Ears negative. Orbits negative. Pharyngeal plexus negative grossly. Osteomyelitis of sella turcica and petrous bone
10. Bouvier[30] 1910	58	Female	Tonsillar abscess left side. Right chronic tonsillitis	Thrombo-phlebitis of left transverse sinus	Left jugular vein thrombosed	None	Lymph node near left jugular vein contained a pus cavity
11. Miadowski quoted in Bouvier[30]	36	Male	Swelling of right side of neck	Purulent meninigitis. Thrombosis of longitudinal, transverse, straight sinuses and vein of Galen	Internal jugular vein	Thrombosis of veins and sinuses	Right mastoid hyperemic

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
12.	Cohn quoted in Bouvier[30]	20	Female	Acute sore throat and swelling of mandibular lymph node	Purulent thrombosis of cavernous sinus	Pus in pterygoid fossa. Phlebitis of deep cervical vein	None	6—7 abscesses in pterygoid muscle and in deep cervical muscles
13.	Kranz 1904 quoted in Bouvier[30]			Chronic right cervical abscess following typhoid and influenza; retropharyngeal abscess	Complete obstruction of all sinuses	Retropharyngeal abscess, pterygoid plexus, cavernous sinus thrombosis	None	The bulb of the jugular vein was free
14.	Oertel[31] 1919	30	Male	Boil on dorsum; retropharyngeal abscess and single abscess in tonsil	Purulent meningitis; purulent thrombosis of cavernous sinus	Nose, along the sheaths of the infra-orbital artery and nerve, right pterygo-maxillary fossa, cavernous sinus	None	Pterygo-maxillary fossa contained abscess. Purulent thrombosis of internal jugular vein
15.	Wylie and Wingrave[14] 1919	48	Female	Right peritonsillar abscess. Cervical phlegmon	Generalized purulent meningitis, pus in cavernous sinus; pituitary liquified; thrombosis of lateral and sigmoid sinuses; necrotizing encephalitis	Not stated by author. Complete necrosis of sphenoid bone	None	Jugular bulb thrombosed. The right orbit contained pus extending into ethmoid

16. Hoston 1920 quoted in Uffenorde[32]	20	Male	Peritonsillar abcess	Thrombosis of cavernous sinus; basal meningitis	Not stated	None	
17. Beck 1914 quoted in Uffenorde[32]			Chronic purulent tonsillitis right and recent left. Retropharyngeal and subpharyngeal abscesses	Purulent meningitis and leptomeningitis; internal pachymeningitis	Not stated	None	Defect of the base of the skull and of the petrous bone
18. Reye[33] 1923	24		Peritonsillar abcess; retropharyngeal abscess	Purulent meningitis and purulent cavernous sinus thrombosis	Angina, thrombophlebitis of right jugular vein. Pyemia, retrograde sinus thrombosis and meningitis	None	Putrid thrombophlebitis of right jugular vein
19. Got[34] 1917	22	Male	Left tonsillitis with tonsillar abscess	Clinical signs of cavernous sinus thrombosis	Thrombophlebitis of tonsillar plexus, pterygoid plexus, foramen ovale, cavernous sinus	None	No autopsy
20. Kernan[35]	18	Male	Peritonsillar abcess	Thrombosis of cavernous and petrous sinuses. Abscess in left temporal lobe	Not stated	None	Abscess in pharyngomaxillary fossa. Thrombosis of internal jugular vein. Mastoids normal
21. Tumpeer and Levinson[36] 1923	7	Male	Tonsillectomy	Meningitis (base free)	Not stated	Yes	Left middle ear contained a drop of thick yellow pus. Ossicles normal. Right ear negative

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
22.	Lyons[37] 1923	31	Female	Acute tonsillitis	Meningitis? Left fronto-parietal abscess	Otitis media	None	Patient recovered
23.	Chisolm and Watkins[38] 1920	40	Female	Alveolar abscess; parotid abscess	Basilar meningitis	Alveolar abscess, pterygoid plexus, cavernous sinus	None	
24.	Chisolm and Watkins[38] 1920	32	Male	Tonsillitis. Retropharyngeal abscess with necrosis	Purulent meningitis and purulent thrombosis of cavernous and lateral sinuses	Empyema of left antrum, pterygoid plexus, cavernous sinus	None	Pus extended along branch III of nerve V through foramen ovale to cavernous sinus
25.	Chisolm and Watkins[38] 1926	25	Male	Tonsillectomy for hypertrophy of tonsils and possible focus of diphtheria bacillus	Basilar meningitis. Thrombosis of both cavernous sinuses	Thrombosis of tonsillar veins, pterygoid plexus, cavernous sinus	None	Paranasal sinus. Middle ear and mastoids normal
26.	Lewin[7] 1926	16		Purulent bilateral tonsillitis; chronic otitis media	Purulent thrombophlebitis of cavernous sinus; chronic choroiditis; bleeding into ventricle	Not stated	Granulation tissue in right cavernous sinus marked. Inflammation around internal carotid	
27.	Lewin[7] 1926	23		Acute and chronic tonsillitis	Clinical meningitis		Tonsils only. Chronic tonsillitis	Patient recovered after tonsillectomy

28. Lewin[7] 1926	80		Phlegmon of left parotid	Purulent gangrenous leptomeningitis and gangrenous thrombosis of cavernous sinus	Not mentioned	None	
29. Fraenkel[39] 1926	32		Purulent tonsillitis	Basilar meningitis. Purulent material in cavernous sinus	Not stated	None	Tonsillar veins, purulent thrombophlebitis
30. Fraenkel[10] 1925	25		Bilateral acute tonsillitis	Cavernous sinus contained pus	Not stated	None	Thrombophlebitis of jugular vein above point of ligation
31. Fraenkel[10] 1925	23		Tonsillar abscess	Local meningitis. Phlebitis of sigmoid sinus and confluence of the sinuses	Not stated	None	Thrombophlebitis of tonsillar and jugular veins
32. Eagleton[11] 1926			Acute inflammation of nasopharynx	General suppurative meningitis; cavernous sinus contained pus	Nasopharynx, septic thrombosis of cavernous sinus, meningitis	None	Vessels at the base of the skull. Antrum free. Mucosa thickened; right frontal sinus obliterated
33. Eagleton[11] 1926	Child		Frequent sore throat otitis media. Abscess in lateral wall of pharynx. Pterygo-maxillary fossa	Meningitis? exudate. Sphenoid sinus contained pus. Purulent necrotizing thrombophlebitis of cavernous sinus	Otitis media, primary thrombosis of jugular bulb. Meningitis; suppuration in pterygo-maxillary fossa, retrograde thrombophlebitis of the pterygoid veins through foramen ovale	None	The left carotid canal contained pus. Nerves and vessels in the foramen lacerum surrounded by pus

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
34.	Eagleton[12] 1927		Male	Abscess in pterygo-maxillary fossa after tooth extraction	Localized meningitis; pus in both cavernous sinuses; extradural abscess in temporo-sphenoidal lobe; sigmoid sinus, pus	Chronic infection of the pterygo-maxillary fossa (dental) thrombophlebitis, through foramen ovale to cavernous sinus. Extradural abscess; localized meningitis of the middle fossa; brain abscess. Retrograde thrombophlebitis of the carotid plexus; suppuration of jugular bulb and sigmoid sinus; purulent otitis and mastoiditis	None	
35.	Eagleton[12] 1927	6	Male	Otitis media. Abcess of pterygo-maxillary fossa. Retropharyngeal abscess	Cavernous sinus filled with pus	Acute otitic pyemia; cavernous sinus by carotid plexus. Secondary abscess of pterygoid maxillary fossa	None	
36.	Schlittler[8] 1929			Peritonsillitis. Phlegmon of para-pharyngeal space	Purulent basal meningitis and pus in cavernous sinus	Phlegmon of parapharyngeal space; phlebitis of the pterygoid pharyngeal plexuses; purulent inflammation of carotid plexus; cavernous sinus; meningitis	Yes	

37. Johnson[43] 1930	7	Male	Severe acute tonsillitis; tonsillectomy.	Brain abscess of right hemisphere.	Not stated.	None	No abscess in cervical glands. Tonsillar fossa clean.
38. Goodyear[44] 1929	18	Male	Peritonsillar abscess.	General suppurative meningitis. Abscess over pituitary gland and cerebellum.	Not stated.	None	Thrombosis of external jugular vein.
39. Elyason[45] 1931	45		Chronic tonsillitis. Peritonsillar abscess.	Purulent meningitis. Brain abscess.	Not stated.		Foramen ovale and foramen lacerum negative. Internal carotid artery and jugular vein not surrounded by pus and not thrombosed.
40. Grabschied[46] 1934	34	Male	Chronic sore throat, peritonsillar abscess, tonsillectomy; 2 years later retropharyngeal abscess.	Purulent internal pachymeningitis of the right cerebral hemisphere.	Retropharyngeal phlegmon, parapharyngeal space; thrombophlebitis of pterygoid plexus. Healing of thrombophlebitis; metastatic pachymeningitic abscess.	None	Sagital sinus empty. Peritonsillar tissue negative. Sinuses of the nose negative.
41. Silverberg[13] 1933	45	Male	Peritonsillar and retropharyngeal abscess	Early exudate. Meningitis; extradural abscess.	Peritonsillar abscess; retropharyngeal abscess; osteomyelitis of base of skull; extradural abscess.	Osteomyelitis of occipital bone. Suppurative inflammation of cervical tissue.	

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
42.	Pollarck[47] 1926	30	male	Purulent tonsillitis; peritonsillar abscess.	Meningo-encephalitis of the middle fossa. Thrombosis of cavernous sinus.	Not stated. Suppurative thrombosis of internal jugular vein extending to base of skull.	None	Parotid abscess and abscess of sternocleidomastoid muscle.
43.	Simeon 1925 quoted in Uffenorde[32]			Tonsillar abscess.	Cavernous sinus thrombosis.	Not stated.	None	Thrombosis of jugular vein.
44.	Hahn[18] 1916	15	Male	Severe lacunar angina.	Purulent meningitis revealed by trephination.			Patient recovered.
45.	Vogel[6] 1933	10		Right peritonsillar abscess; otitis media; cervical abscess.	Basal leptomeningitis with purulent external and internal pachymeningitis of the right middle fossa. Cortical abscess of right temporal lobe.	Not stated by author. Purulent lymph angitis of the sheaths of the right internal carotid. Suppurating thrombophlebitis of the branches of facial vein.		Right acoustic nerve covered with pus.
46.	Vogel[6] 1933	19		Swelling of left temporal region.	Complete suppuration of cavernous sinus and purulent thrombosis of sigmoid sinus.	Purulent thrombophlebitis of left jugular vein and of veins of pterygomaxillary fossa.	None	Purulent thrombophlebitis of bulb of jugular vein.
47.	Vogel[6] 1933			Purulent tonsillitis; septum abscess of nose; temporal abscess.	Old basal meningitis; recurrent temporal lobe abscess.		None	

48. Wessely[2] 1931	44		Right purulent tonsillitis; gangrenous parotitis.	Exudative pachymeningitis.	Not stated.	Hyperemia of lymph node.	Purulent infiltration of Masseter, temporal and pterygoid muscles.
49. Wessely[3] 1932	57	Male	Peritonsillar abscess.	Basal meningitis; purulent thrombophlebitis of cavernous sinus.		None	Abscess in pterygoid muscle. Periarticular phlegmon. Sella turcica filled with pus.
50. Wessely[3] 1932	55		Tonsillitis; pus in pterygoid muscle.	Purulent leptomeningitis; purulent thrombosis of cavernous and intracavernous sinuses.	Small veins of pterygoid plexus partially thrombosed; pus spread to base of skull.	None	
51. Wessely[3] 1932	29	Male	Tonsillitis; tonsillar abscess bilateral; left purulent pharyngitis.	Basal meningitis of middle cerebral fossa.		None	Phlegmonous inflammation of anterior mediastinum up to the cardium.
52. Wessely[3] 1932	18		Tonsillitis; tonsillectomy; tonsilar abscess; retropharyngeal and parapharyngeal space; small abscesses.	Purulent basal meningitis; fibrinopurulent pachymeningitis; purulent thrombosis of both cavernous sinuses.	Phlegmon from tonsil to anterior pharyngeal wall; parapharyngeal space upwards to base of skull infiltrating pterygoid muscle, along third branch of trigeminal nerve and middle meningeal artery through foramen spinosum to middle cerebral fossa.	Yes	Purulent autolyses of the sheaths of the vessels of left side of neck.

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
53.	Shapiro[7] 1930			Tonsillectomy; swelling of mandibular angle.	Basal meningitis.	Pus around carotid sheath.	None	
54.	Ide[49] 1929	10		Tonsillectomy.	Cavernous sinus thrombosis.	No autopsy report.		
55.	Parry[50] 1909			Tonsillectomy and adenoidectomy; otitis media and suppurating mastoiditis.	Meningitis; cerebellar abscess.	Middle ear and mastoid.	None	
56.	Housden[51] 1929			Acute tonsillitis	Abscess of brain	Not stated	None	
57.	Claus[52] 1929			Tonsillitis	Serous hemorrhagic meningitis; thrombophlebitis of cavernous and transverse sinuses	Thrombophlebitis of jugular vein	None	Thrombophlebitis of ophthalmic vein
58.	Knick 1923 quoted in Uffenorde[32]			Tonsillectomy. Parapharyngeal phlegmon	Thrombosis of the transverse sinus	Not stated	None	Thrombophlebitis of internal jugular vein above the junction with the facial vein
59.	Meslin and le Barazer[53] 1925	13	Male	Tonsillitis and tonsillar phlegmon bilateral	Clinical signs of cavernous sinus thrombosis	Not mentioned	None	No autopsy. Abscess of jugular vein with spontaneous rupture through the skin

60. Seggel[54] 1907	20	Male	Right tonsillitis. Swelling of right side of neck	Clinical signs of cavernous sinus thrombosis	Right purulent tonsillitis and thrombophlebitis of palatine vein; internal jugular vein; inferior petrosal sinus; right cavernous sinus; circular sinus; left cavernous sinus	None	Recovered. Amaurosis bilateral
61. Comer[55] 1931	10	Male	Subacute tonsillitis right. Tonsillectomy. Cellulitis of neck and face	Clinical signs of cavernous sinus thrombosis			No autopsy report
62. Malan[56] 1930	25	Male	Acute tonsillitis; right and left peritonsillar phlegmon	Purulent basal meningitis. Pus in fourth ventricle. Purulent and gangrenous thrombophlebitis of cavernous and circular sinuses. Extradural abscess	Tonsillitis; left peritonsillar abscess; parotid abscess; infection of tonsillar and pterygoid plexuses; cavernous sinus	None	Pterygomaxillary fossa free of pus; internal jugular vein normal; obliterating thrombophlebitis of the pterygoid plexus
63. Banti quoted in Malan[56]		Female	Tonsillar abscess	Thrombophlebitis of both lateral sinuses and longitudinal sinus	Tonsillar abscess; thrombophlebitis of jugular vein; both lateral sinuses and longitudinal sinus	None	Clinical; Jacksonian epilepsy

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
64.	Ferretti[16] 1927	40	Male	Right lacunar tonsillitis; peritonsillar phlegmon	Brain abscess of the inferior portion of the pre- and post-Rolandic areas	Speculative; infection of lateral pharyngeal lymphatics; deep cervical lymph nodes; ascending endocranial lymphatics in the perivascular sheath of the Sylvian artery	None	No autopsy
65.	Ameriso[1] 1935	19	Male	Tonsillitis	Basal meningitis and septic infarct of the pituitary; thrombophlebitis of cavernous sinus	Tonsillar veins; pterygoid plexus; vein of foramen ovale and cavernous sinus, or interior juglar vein; inferior petrosal and cavernous sinuses	Very careful examination	Acute desquamative lymphademitis and necrotic thrombophlebitis of the interior jugular vein; septic sinusitis of the sphenoidal sinus; thrombosis of carotid artery; purulent periarteritis of the cavernous portion of the interior carotid
66.	Calamida[57] 1930	61		Peritonsillar abscess following tooth extraction. Ulcerative and necrotizing tonsillitis	Hemorrhagic purulent generalized meningitis. Pus in cavernous sinus. Thrombosis of superior longitudinal sinus	By Vasa Vasorum of the large vessels to the cavernous sinus; suppuration of longitudinal sinus. Infection traveled from the jugular to pterygoid, pharyngeal and peripharyngeal plexuses	None	Pus extended along the middle meningeal also

67. Campbell[58] 1932	35	Female	Peritonsillar abscess following tonsillectomy	Clinical signs of cavernous sinus thrombosis	Septic thrombophlebitis of the pterygoid plexus; deep facial branch to facial vein; angular and ophthalmic veins to cavernous sinus	None	Partial autopsy. No brain post
68. Claus[59] 1928	31	Male	Bilateral tonsillitis; tonsillectomy	Thrombosis of cavernous sinus and the pial veins; purulent meningitis	Retrograde thrombosis. Purulent liquefaction of the pterygoid plexus and thrombosis of the larger veins by way of the ophthalmic vein to the cavernous sinus; thrombosis of the pial veins; meningitis	None	
69. Claus[59] 1928	31	Male	Frequent angina. Tonsillectomy	Purulent thrombosis of cavernous sinus and transverse sinus. Hemorrhagic meningitis	Retrograde by way of the pterygoid plexus and ophthalmic vein	None	Ligation of the internal jugular vein. At autopsy pus was found in the jugular vein above the point of ligation and in the right inferior ophthalmic vein
70. Blachez[60] 1880		Male	Phlegmonous tonsillitis. Swelling of cervical region; tonsillar abscess	All cerebral sinuses contained pus	Not mentioned especially	None	The tonsillar veins were filled with pus

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
71.	Sicard[61] 1934	41	Male	Cervical abscess; latent otitis media	Generalized meningitis. Pus in ventricles	Otitis-mastoiditis; internal auditory canal contained pus	None	Author states that the cervical abscess is secondary to a purulent otitis media; pus traveled down along the digastric and sternocleido mastoid muscles. Cervical region not examined; autopsy restricted to head
72.	Mitvalsky[62] 1896	56	Male	Phlegmonous gangrenous tonsillitis	Thrombophlebitis of the anterior cerebral sinuses	Gangrenous tonsillitis; pterygoid plexus; base of skull; small vein of the foramen ovale; cavernous sinus; ophthalmic veins	None	Purulent thrombophlebitis of the orbital veins. The sphenoid body infiltrated with pus. Purulent periostitis of left lower jaw
73.	Podesta [63] 1927	17	Male	Acute purulent tonsillitis; retropharyngeal abcess	Basal fizrinous leptomeningitis. Purulent thrombosis of circular sinus	Tonsillar vein pterygoid plexus-anastomosing branches	None	Purulent thrombosis of left ophthalmic vein; jugular vein and lateral sinus negative. Ethmoidal, sphenoidal and frontal sinuses negative
74.	Ogle[64] 1865	39	Male	Sore throat with abscess formation (location?)	Purulent thrombosis of both cavernous sinuses localized. Basal meningitis	—	None	Pus in both orbital cavities and thrombosis of the orbital vessels

75. Fauvel 1887 quoted in Terson[11]	28	Female	Left phlegmonous tonsillitis; abscess of right tonsil	Suppuration of cavernous sinus	Pterygoid plexus-vein of foramen ovale; cavernous sinus	None	Thrombosis of ophthalmic veins
76. Jenneman[65] 1935	37	Female	Tonsillitis and peritonsillitis	Clinical signs of meningitis	—	None	Patient recovered
77. Jenneman[65] 1935	27	Female	Tonsillitis	Clinical signs of meningitis	—	None	Patient recovered
78. Jenneman[65] 1935	42	Female	Acute tonsillitis	Clinical signs of meningitis	—	None	Patient died. No autopsy
79. Schubel quoted in Jenneman[65]	2		Peritonsillar phlegmon	Meningitis; thrombosis of cavernous sinus	Peritonsillar abscess and of parotid loge; by venous channels to cavernous sinus	None	Perforation of abscess into the external auditory canal
80. Siemerling quoted in Jenneman[65]	15	Male	Tonsillitis	Clinical signs of meningitis	—	None	Patient recovered
81. Terson[11] 1893	39	Male	Abscess in left parotid region and submaxillary region	Acute hyperemia of meninges. Purulent thrombophlebitis of both cavernous and circular sinuses	Diffuse osteoperiostitis of the inferior maxilla; purulent thrombophlebitis of the pterygoid plexus-thrombophlebitis of vein of foramen ovale; cavernous sinus; orbital phlebitis	None	Tonsils negative. The base of the skull negative. Pyramids normal; the veins at the base of the skull filled with pus. The parotid and temporal pockets revealed disappearance of the muscle elements and was replaced by a sanguinous fluid
82. Ucherman[66] 1907			Cervical abscess	Purulent pachymeningitis	The inflammation followed along the path of the large vessels	None	Phlebitis of the left jugular vein. Pus behind the left ocular bulb

TABLE I—(Continued)

No.	Reference	Age	Sex	Primary Lesion	Changes in Venous Sinuses, Brain and Meningitis	Suggested Mode of Spread of Infection	Microscopic Examination	Remarks
83.	Ucherman[67] 1907	18	Female	Retropharyngeal abscess; cervical abscess	Edema of the brain. Thrombosis of confluence of the sinuses	According to Gruenwald. Pterygoid palatine fossa; pterygoid plexus; occipital veins	None	The retropharyngeal abscess extended to the base of the skull. Hyperemia of mastoid and a few purulent cells. Four years ago abscess in lymph nodes below both ears
84.	Dixon [68] 1930	30	Female	Sore throat; purulent cellulitis of deep tissues of the neck	Purulent basilar meningitis	—	Only from jugular vein	Left jugular bulb and the jugular vein filled with septic thrombi
85.	Dixon[68] 1930	19	Female	Acute sore throat	Suppuration of the pituitary and thrombosis of the cavernous sinus	—	None	The internal jugular vein revealed marked inflammation, fibrotic thickening of the wall. Small purulent thrombi in the lymphatics
86.	Günther[69]	20	Male	Chronic tonsillitis; tonsillectomy and adenoidectomy; cervical phlegmon	Purulent basal and generalized meningitis	Purulent osteomyelitis of the dens epistropheus and perforation into the upper vertebral canal	None	Purulent arthritis between the atlas and the epistropheus
87.	Teissier Boudon and Duvoir[70]	20	Male	Angina; scarlet fever; angina	Generalized meningitis and purulent spinal meningitis	—	None	The bones of the skull, the cribriform plate, the petrous bone and the internal ear and mastoids were negative

TABLE II

One injection of 1 cc. of a 48-hour broth culture of microrganisms into the sheath of the right internal carotid artery.

No. of Adult Dogs	Material Injected	Time of Survival		Inflammation		
		No. of Dogs Died	No. of Dogs Killed	of the sheath of the internal carotid artery at its cervical portion	in other regions found in	Meningitis
5	Human strain of pneumococci IV, 2 dogs Human strain of hemolytic streptococci, 2 dogs	2 dogs (human strain) after 5 and 7 days		1 dog which died after 5 days 1 dog which was killed after 4 weeks	.....	.....
	Concentrated broth of hemolytic streptococci obtained from dogs, 1 dog	1 dog (concentrated streptococci) after 7 days	2 dogs after 4 weeks			
6	Hemolytic streptococci obtained from dogs plus a few drops of india ink	2 dogs after 1 and 6 days	2 dogs after 1 and 2 weeks 2 dogs after 4 weeks	1 dog which died after 1 day 1 dog which died after 6 days 1 dog which was killed after 2 weeks	.....	.....

TABLE III

The sheaths of the right and left internal carotid arteries were injected. One cc. of a 48-hour broth culture of microorganisms was injected once into the sheath of the right internal carotid artery and, 3 to 6 weeks later, one cc. of a mixture of broth culture of similar organisms with either india ink or a few drops of a 2½% solution of gum tragacanth, or one cc. of india ink alone was injected into the sheath of the left internal carotid artery.

No. of Adult Dogs	Material Injected	Time of Survival		Results	Meningeo-encephalitis
		No. of Dogs Died	No. of Dogs Killed	Inflammation of the sheath of the left internal carotid artery at its cervical portion	
10	Right—hemolytic streptococci (human strain), 1 dog; hemolytic streptococci (dog), 1 dog	.....	1 dog, after 24 hours	Positive	Negative
	Left—india ink, 3 to 6 weeks later—both of these dogs		1 dog, after 48 hours		
	Right—hemolytic streptococci (human strain) plus a few drops of india ink	.....	1 dog, after 2 weeks	Negative	Negative
	Left—hemolytic streptococci (dog) plus india ink, 3 weeks later—1 dog				
	Right—hemolytic streptococci (dog) plus india ink				

Left—hemolytic streptococci (dog) plus a few drops of gum tragacanth, 4 weeks later—1 dog	.....	1 dog, after 2 weeks	Positive	Negative
Right—hemolytic streptococci (dog)				
Left—hemolytic streptococci (dog) plus a few drops of gum tragacanth, 3 weeks later—1 dog	.....	1 dog, after 2 weeks	Positive	Positive
Right—concentrated broth of hemolytic streptococci (dog)	.....	5 dogs, after 2 weeks	Positive 2 dogs Negative 3 dogs	Negative
Left—concentrated broth of hemolytic streptococci (dog) plus a few drops of gum tragacanth, 3 weeks later—5 dogs				

TABLE IV

Injection into the sheath of one or both internal carotid arteries of 1 cc. of a 24-hour broth culture of hemolytic streptococci obtained from dogs, with or without admixture of a few drops of a 2½% so'ution of gum tragacanth.

No. of Dogs (puppies)	Material Injected	Time of Survival: No. of Dogs Died	No. of Dogs Killed	Results: Inflammation of the sheath of the internal carotid artery in its cervical	petrous portions	cavernous
10	Right—hemolytic streptococci—6 dogs	1 dog after 2 hours		Neg. (bac.)	Negative	Negative
		1 dog after 3 days		Positive	Negative	Negative
		1 dog after 5 days		Negative	Negative	Negative
		1 dog after 10 days		Negative	Negative	Negative
		1 dog after 10 days		Positive	Negative	Negative
		1 dog after 12 days		Negative	Negative	Negative
	Right — concentrated broth of hemolytic streptococci—4 dogs	1 dog after 2 hours		Pos. (bac.)	Negative	Negative
		1 dog after 4 days		Positive	Positive	Positive
		1 dog after 8 days		Positive	Negative	Negative
		1 dog after 9 days		Negative	Negative	Negative
9	Right—hemolytic streptococci	1 dog after 2 hours		Negative	Negative	Negative
	Left—hemolytic streptococci plus a few drops of gum tragacanth, 3 weeks later—7 dogs	1 dog after 1 day		*Pos. (bac.)	Negative	Negative
		1 dog after 4 days		Negative	Negative	Negative
		1 dog after 4 days		Negative	Negative	Negative
		1 dog after 4 days		*Pos. (bac.)	Negative	Pos. (bac.)
		1 dog after 11 days		Negative	Negative	Negative
		1 dog after 11 days		Negative	Negative	Negative
	Right — concentrated broth of hemolytic streptococci	1 dog after 4 days		*Pos. (bac.)	Pos. (bac.)	Negative
	Left — concentrated broth of hemolytic streptococci, plus a few drops of gum tragacanth, 3 weeks later—2 dogs		1 dog after 5 weeks	Negative	*Positive	*Positive

*Positive left internal carotid artery.

BIBLIOGRAPHY

1. Wessely, E. Die endocranielle Komplikation nach Peritonsillitis. Ztschr. f. Hals-, Nasen- u. Ohrenh., 9:439, 1924.

2. Wessely, E.: Ein Weiterer Beitrag zur Entstehung der endokraniellen Komplication nach Tonsillitis und Peritonsillitis. Ztschr. f. Hals-, Nasen- u. Ohrenh., 28:167, 1931.

3. Wessely, E.: Die endocranielle Komplication nach Tonsillitis und Peritonsillitis. Eine Clinsche Studie. Monatschr. f. Ohrenh, 66:1190, 1932.

4. Ameriso, J.: Tromboflebitis del seno cavernoso por amigdalitis. Rev. Med. del Rosario, 25:499, May, 1935.

5. Shapiro, S. L.: Deep Cervical Infection Following Tonsillectomy; Report of 300 Cases with Review of the Literature. Arch. Otolaryng., 11:730, 1930.

6. Vogel, K.: Aufsteigende Infektion des Endocraniums bei tonsillogener Rachenplegmone. Ztschr. f. Hals-, Nasen- u. Ohrenh., 33:4, 1933.

7. Lewin, R.: Beitrag zur Klinik einiger endokranieller Komplicationen, von Rachen und Mund höhle ausgehend. Beitr. z. prakt. u. Theoret. Hals-, Nasen- u. Ohrenh., 23:31, 1926.

8. Schlittler, E.: Ueber tödliche Komplicationen im Verlaufe der Angina lacunaris. Schweiz. Med. Wchnschr., 59:29, 1929.

9. Panas, P.: Diagnostique d'une thrombose des veines ophthalmiques et des sinus caverneux. La Semaine Médicale., 5:255, 1885.

10. Festal: Thèse de Paris. 1887. Quoted by Panas.

11. Terson, A.: Rémarques sur les phlebites orbitaires. Recueil d'Opht., 15:650, 1893.

12. Dietrich, A.: Handbuch der speziellen pathologischen Anatomie und Histologie. Henke and Lubarsch., Vol. 4, Part I. Julius Springer, 1926.

13. Silverberg, J. S.: Peritonsillar Abscess; Retropharyngeal Abscess; Osteomyelitis of Base of Skull; Extradural Abscess and Death. Report of Case. Laryngoscope, 43:835, 1933.

14. Wylie, H. and Wingrave, W.: Peritonsillar Abscess Followed by Osteomyelitis, Necrotizing Encephalitis and Meningitis. Lancet, 1:178, 1919.

15. Macewen, W.: Pyogenic Infective Diseases of the Brain and Spinal Cord; Meningitis, Abscess of Brain, Infective Sinus Thrombosis. Glasgow, J. Maclehose and Sons, 1893.

16. Ferretti, C.: Su una rara complicanza del flemone peritonsillare. Arch. Ital. di Otol., 38:463, Aug. 1927.

17. Turner, A. L. and Reynolds, F. E.: Study of Paths of Infection to Brain, Meninges and Venous Blood Sinuses from Neighboring Peripheral Foci of Inflammation. J. Laryng. & Otol., 41:717, 1926.

18. Ferron, M.: Note sur la constitution des parois du sinus caverneux et les rapports des nerfs oculomotor et trijumeau avec ses parois externe et superieure. Jour. de Med. de Bordeaux, 43:88, 1913.

19. Testut, L. and Latarjet, A.: Traité d'Anatomie humaine Eighth edition, Vol. IV, Appareil de la Digestion, page 136. Gaston Doin & Cie, 1931.

20. Hall, C.: The Parapharyngeal Space: An Anatomical and Clinical Study. Annals of Otology, Rhinology and Laryngology, 43:793, 1934.

21. Steinberg, B. and Goldblatt, H.: Studies on Peritonitis. Arch. Int. Med., 39:446, 1927.

22. v. Stein, S.: Der erste publicirte Fall eine pharingitis phlegmonosa acuta durch eine Meningitis purulenta complicirt. Monatschr. f. Ohrenh., 28:313, 1894.

23. De La Personne: Phlébite Suppurée des Veines ophthalmiques et des Sinus caverneux. Arch. d'Opht., 5:436, 1885.

24. Zawadski: Septicopyaemia nach Zahnextraktion. Zentralbl. f. Chir., 13:894, 1886.

25. Riese, H.: Thrombophlebitis der Sinus durae matris selteneren Ursprungs. Arch. f. Klin. Chir., 61:839, 1900.

26. Tollens, C.: Angina and Pharyngitis phlegmonosa mit eitriger Thrombose des Sinus cavernosus und eitriger Meningitis basilaris. Ztschr. f. Ohrenh., 44:(3) 225, 1903.

27. Davis, H. J.: Chart and Brief Notes of a Case of Cavernous Sinus Thrombosis Following Left Tonsillitis in a Boy Aged 10; Fatal Termination in Eighteen Days. Proc. Roy. Soc. Med., Laryngological Section, 174, 1913.

28. Proskauer, A.: Seltene Komplication eines Tonsillar Abscesses. Berliner Klin. Wchnschr., 51: Part I, 1241, 1914.

29. Jacques and Lucien: Phlegmon Périamygdalien Mortel par thrombophlébite du sinus caverneux. Soc. Franc. d'Otorhino. Laryng., 24:Part II, 146, 1908.

30. Bouvier, P.: Thrombose der Vena jugularis interna und des Sinus transversus nach Angina und Drüsenabszess. Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres., 4:26, 1910.

31. Oertel, B.: Beitrage zur Thrombose des Sinus cavernosus. Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres., 13:183, 1919.

32. Uffenorde, W.: Die Verwicklungen der akuten Halsentzündungen unter besonderer Berücksichtigung der Beteiligung des Spatium parapharyngeum. Ztschr. f. Laryng., 13:357, 1925.

33. Reye: Zur Klinik und Atiologie der postanginösen septischen Erkrankungen. Virchows Arch. f. Path. Anat., 246:22, 1923.

34. Got: Les thrombo-phlébites du sinus caverneux. Rev. de Laryng., 38:313, 1917.

35. Kernan, J. D.: Case of Lateral Sinus Thrombosis with Bacillus Proteus in Blood Culture and in the Thrombus. Laryngoscope, 31:384, 1921.

36. Tumpeer, I. H. and Levinson, A.: Fatal Infections Following Tonsillectomy. J. A. M. A., 80:20, 1923.

37. Lyons, H. R.: Unusual Complications of Acute Tonsillitis. J. A. M. A., 81:1605, 1923.

38. Chisolm, J. J. and Watkins, S. S.: Twelve Cases of Thrombosis of Cavernous Sinus, from a Study of 50,000 Surgical Histories in Johns Hopkins Hospital. Arch. Surg., 1:483, 1920.

39. Fraenkel, E.: Pyemia After Tonsillitis. Deutsche med. Wchnschr., 52:93, 1926.

40. Fraenkel, E.: Über postanginöse Pyämie. Virchows Arch. f. path. Anat., 254:639, 1925.

41. Eagleton, W. P.: Cavernous Sinus (Thrombophlebitis and Allied Septic and Traumatic Lesions of the Basal Venous Sinuses): A Clinical Study of Blood Stream Infection. Macmillan, 1926.

42. Eagleton, W. P.: Carotid Venous Plexus as Path of Infection in Thrombophlebitis of Cavernous Sinus; Its Relation to Retropharyngeal and Sphenoidal Suppuration. Arch. Surg., 15:275, 1927.

43. Johnson, W.: Cerebral Abscess Following Tonsillar Infection. Brit. M. J., 2:13, 1930.

44. Goodyear, H. M.: Peritonsillar Abscess, Thrombosis of the External Jugular Vein, and Brain Abscess. Laryngoscope, 39:674, 1929.

45. Elyason, M. I.: Intracranial Complications of Peritonsillar Abscess. Vrach. Gaz., 20:1510 (Oct.), 1931.

46. Grabschied, E.: Ein Beitrag zur endokranillen Komplication nach Rachenphlegmone. Klin. Wchnschr., 13:1017, 1934.

47. Pollark, R.: Meningo-Enzephalitis, Pachymeningitis der mittleren Schädelgrube, Thrombose der Vena jugularis interna und des Sinus cavernosus nach eitriger Peritonsillitis. Wien. Med. Wchnschr., 7611:1328, 1926.

48. Hahn, F.: Meningitis nach Angina; Trepanation; Heilung. München. Med. Wchnschr., 63, Part 2, 1822, 1916.

49. Ide, C.: Cavernous Sinus Thrombosis and Meningitis Following Tonsillectomy. Arch. Otolaryng., 9:656, 1929.

50. Parry, L. A.: A Case of Acute Mastoiditis With Lateral Sinus Suppuration and Cerebellar Abscess as Complications of the Operation for the Removal of Tonsils and Adenoids. Lancet, 1:1821, 1909.

51. Housden, E. G.: Cerebral Abscess Following Acute Tonsillitis. Brit. M. J., 1:1158, 1929.

52. Claus, G.: Komplicationen bei und nach der submucösen Septumresektion: Ztschr. f. Hals-, Nasen- u. Ohrenh., 23:444 (Sept.), 1929.

53. Meslin and Le Barazer: Un Cas de Thrombo-phlébite des Sinus caverneux-transverse lateral et de la Jugulaire informe à forme pyohémique, d'origine amygdalienne. Rev. de Laryng., 46:639, 1925.

54. Seggel, K.: Erblindung infolge Tonsillitis phlegmonosa auf dem Wege der Thrombosinusitis cerebralis. Klin. Monatsbl. f. Augenh., 45, Part 2, 129, 1907.

55. Comer, M. C.: Cavernous Sinus Thrombosis in Child Following Tonsillectomy. Arch. Otolaryng., 13:733, 1931.

56. Malan, A.: Thromboflebite del seno cavernoso consecutiva a flemmone peritonsillare. Arch. Ital. di Otol., 41:1 (Jan.), 1930.

57. Calamida, U.: Trombosi del seno cavernoso e del seno longitudinale superiore consecutive ad ascesso peritonsillare. Osp. Maggiore, 18:57, 1930.

58. Campbell, E. H.: Cavernous Sinus Thrombophlebitis Following Tonsillectomy. Report of Case. Annals of Otology, Rhinology and Laryngology, 41:170, 1932.

59. Claus, H.: Achtundzwanzig Fälle von Pyämie nach Angina. Ztschr. f. Hals-, Nasen- u. Ohrenh., 21:114, 1928.

60. Blachez: Phlébites compliquant certaines affections de la face. J. de Med. et Chir. Prat., 51:7, 1886.

61. Sicard, A. and Brunhes, J.: Abcés cervicaux compliqués de méningite mortelle (otite méconnue à Pneumococcus mucosus. Presse Med., 42:308, 1934.

62. Mitvalsky: Contribution à la connaissance de la thrombophlébite orbitaire. Arch. d'Opht., 16:22, 1896.

63. Podesta, E.: Tromboflebite del seno cavernoso e del seno coronario in pariente con inferione tonsillare ed ascesso retrofaringeo. Valsalva 3:409 (Sept.), 1927.

64. Ogle, J. W.: Cases Illustrating the Formation of Morbid Growths, Deposits, Tumors, Cysts, etc., in Connection With Brain and Spinal Cord and Their Investing Membranes. Brit. & Foreign Medico—Chir. Rev., 36:200-491, 1865.

65. Jenneman, F.: Meningitis bei Angina. Ztschr. f. Laryng., Rhin., Otol., 26:372, 1936.

66. Uchermann, V.: Die otogene Pyämie und infektiöse Sinus Thrombose. Arch. f. Ohrenh., 71:237, 1907.

67. Uchermann, V.: Ein supponierter Fall von otogener Encephalitis toxica. Arch. f. Ohrenh., 74:87, 1907.

68. Dixon, I. J. and Helwig, F. C.: Thrombophlebitis of the Internal Jugular Vein as a Complication of Tonsillitis. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 39:1137, 1930.

69. Günther, K.: Vier Jahre Tonsillektomie an der Würzburger Universitätsklinik für Ohren - Nasen und Kehlkopfkranke. Ztschr. f. Laryng. & Rhin., 17:191, 1928.

70. Teissier, Boudon and Duvoir: Reference not available.

LXXVII

THE TENSOR TYMPANI MUSCLE AND ITS RELATION TO SOUND CONDUCTION*

ERNEST GLEN WEVER
AND
CHARLES W. BRAY

PRINCETON, N. J.

The tensor tympani muscle was discovered by Eustachius in 1564.[1] Since that time there has been much discussion of its function in hearing. Three types of theory have been proposed. These are (1) the intensity-control theory, (2) the frequency-selection theory, and (3) the fixation theory.

The intensity-control theory holds that the tensor tympani muscle by its degree of contraction alters the efficiency of transmission of sound by the middle ear system. This theory in its most complete form supposes that under appropriate conditions the efficiency may be either increased or decreased.[2] The theory in a more limited form, known as the protection theory, supposes that efficiency can be changed only in the negative direction. According to this theory, the muscle acts so as to safeguard the inner ear against stimuli of excessive magnitude.[3]

According to the frequency-selection theory, the action of the tensor tympani muscle may cause certain tones to be favored over others in transmission.[4] This theory has usually been called the accommodation theory in a fancied analogy with the operation of the ciliary muscle in vision, but the analogy is hardly a direct one and the name is therefore confusing.

The fixation theory assumes that the muscle merely acts so as to maintain the drum and ossicles in a constant state of tension, and thereby aids in the transmission process. This theory denies any differential action of the muscle.[5]

The development of these theories, and the arguments that have been advanced regarding them, form an interesting historical subject, but one that cannot be treated fully here.[6] The frequency-selection

*From the Princeton Psychological Laboratory. This investigation was aided by a grant from the National Research Council.

theory had considerable vogue for a time, but now has largely been given up in favor of the protection theory.[7]

Three forms of evidence have been brought forward in relation to the above theories. Most of the discussions, both early and late, have been based upon observations of the anatomical relations within the middle ear and the conditions of stimulation of the tensor tympani muscle. Further data have been added by the subjective observation of the effects of contractions of the muscles on the loudness of sounds. Finally, attempts have been made to determine by direct measurements the effects on sound transmission either of reflex contraction of the muscle or of artificial tension on its tendon. This last type of investigation is the particular interest of the present paper.

Politzer[8] in 1864 first sought to determine the effects of tensor contraction by direct measurements. He recorded mechanically the movements of the head of the malleus in freshly killed dogs during stimulation of the ear by sounds, both under normal conditions and during electrical excitation of the fifth cranial nerve. He found that the recorded movements were reduced to about one-third when excitation of the nerve caused contraction of the tensor tympani muscle. In experiments on the heads of cadavers he observed reductions of movements when strong tension was exerted upon a thread tied to the tensor tympani muscle. In further experiments on dogs, in which an auscultation tube from the bulla was substituted for mechanical recording, he observed that stimulation of the fifth nerve caused the fundamental tone of a tuning fork to be weakened and the overtones to come out more clearly.

Later in the same year, Lucae[9] reported similar experiments. He used fresh human heads, and recorded the movements of the drum and ossicles during stimulation by bone-conducted sounds. A string was attached to the tensor tympani muscle, and then was run over a pulley to various weights. Smaller amplitudes of vibration were recorded when the weights were added, and the reduction was described as proportional to the tension. Other observations indicated that the tone became "dull" as a result of drum tension, and Lucae concluded that such tension caused deep tones to be better "accommodated."

Mach and Kessel[10] in 1872 also worked on cadavers, and observed through a microscope the movements of metallic particles placed on the head of the malleus. As in Lucae's experiments, a thread was tied around the tensor tympani muscle and run over a pulley to a weight. Mach and Kessel observed that the ossicular movements set

up by a low note from an organ pipe were reduced from 5 to 3 arbitrary units when a tension of 3 grams was applied. High tones were less affected.

The above experiments were obviously limited by the methods used for registering the movements of the ossicular system. Mechanical registration is insensitive, and it also interferes with the normal movements of the parts. The auscultation method, which was also tried, introduces the ear of the experimenter, and is also insensitive to changes of intensity. It is therefore not surprising that the experiments yielded discordant results.

In 1931, Crowe and Hughson[11] first reported experiments in which the electrical responses of the ear were used to determine the effects of tension on the tensor tympani tendon. In etherized cats the bulla was opened ventrally to expose the middle ear, and a hook was placed around the tendon of the tensor tympani muscle. From the hook a thread was led out of the ventral opening of the bulla and over a pulley to a scale pan. The electrical responses resulting from acoustical stimulation of the ear were observed by listening in a telephone receiver. Observations were made before and after the application of weights, and it was found that loading caused a reduction of responses. A tension of 10 grams reduced the responses to speech sounds and all low tones, and 50 grams eliminated these tones under the conditions of observation. High tones were less affected.

In the present investigation also the electrical responses of the cochlea were used to study the effects of tension on the tensor tympani tendon. The procedure differed from that of Crowe and Hughson particularly in the method of application of tension and in the means of recording the electrical responses.

METHOD AND PROCEDURE

The method of exposure of the tensor tympani muscle and tendon was the same as that described by Crowe and Hughson, and earlier by Heidenhain.[12] With the cat supine, the bulla was approached through an incision in the throat, and opened to expose the round window and septum. The septum was removed to expose the dorso-lateral portion of the middle ear, with the drum, malleus, and tensor tympani muscle in clear view.

The method of applying tension to the tendon which was used by Crowe and Hughson does not exactly reproduce the action of the muscle. The normal direction of pull is dorso-medial and slightly forward, while the direction of pull of a thread that is attached to

the muscle and led directly out of the bulla as described is ventral and thus more than 90° from the normal. Since the muscle remained attached to the roof of the bulla, the effective direction of pull on its tendon was somewhere between the normal and the ventral directions; the exact direction is difficult to estimate, as it would depend upon the place and manner of inserting the hook, and also upon the degree of tension.

In the present study it was considered desirable to obtain a normal direction of pull. The technique that was adopted after considerable experimentation was as follows:

A fine silk thread was tied around the tensor tympani tendon. This was accomplished with the aid of two instruments, a thread carrier of soft copper wire and a hook of fine steel wire. The thread carrier was given a rounded end by momentarily holding it in a flame, and was bent to permit passing it alongside the drum and partially around the tendon. One end of the thread was cemented to the end of the carrier, and thus passed beneath the tendon, where it was caught from the other side with the hook and a loop pulled upwards. The thread carrier was retracted and the thread cut loose, whereupon the loop was pulled through with the hook. The end of the thread was tied about the standing part in a slip-knot, and the knot carefully guided downward and finally pulled snugly around the tendon. In these manipulations extreme care was of course necessary to avoid damage.

To obtain the proper direction of pull it was necessary to have a pulley within the middle ear cavity. The pulley that was found most suitable was a glass tube, pulled out to a small tapering form at one end and bent to a rounded angle of about 90° near the tip. The thread was passed through the tube, and the tube, held by an adjustable stand, was lowered to position just above the belly of the muscle. From the tube the thread ran upwards over a large wooden pulley to a scale pan. The friction of the whole system was measured and found to be 0.5 gram or less, and therefore negligible.

The animal was stimulated with pure tones between 300 and 10,000~, at various intensities. By means of a calibration with a condenser microphone, the intensities were known in absolute units, in terms of sound pressure.[13]

The electrical responses from the cochlea were picked up by a silver-foil electrode on the membrane of the round window and an indifferent electrode in inactive tissue at the edge of the wound. The potentials were amplified and led to a recording instrument.

Two recording instruments were used, a cathode-ray oscillograph and a selective vacuum-tube voltmeter (General Radio Co. Type 636-A Wave Analyzer). The latter instrument has great advantages for the measurement of single frequencies. Its high degree of selectivity results in the elimination of all background noises except those that fall within a few cycles of the response that is being measured, so that a degree of sensitivity far greater than usual can be realized. Both instruments were calibrated in connection with the amplifier, so that the responses as picked up at the round window could be calculated in microvolts.

Other details of procedure varied somewhat in different experiments, as described below. The experiments were performed on six cats under urethane anesthesia.

RESULTS

The following method was used to determine the effect of different degrees of tension upon the responses to particular tones. The animal was stimulated with a tone of a given frequency and intensity, and during the stimulation successive weights were placed on the scale pan, and measurements made of the responses. Before and after application of each weight the scale pan was lifted and normal responses observed. The control measurements thus alternated with the measurements for various weights. The weights regularly used were 2, 5, 7, 10, 15, and so on by five-gram steps to fifty or sixty grams, but in the records the weight of the scale pan, one gram, has been added to these figures.

Results which are typical of those obtained by this procedure are shown in Fig. 1. The stimulating tone had a frequency of 700~ and an intensity of 10 bars, and normally gave a response of about 140 microvolts (μv.), as indicated by the dotted curve, marked "base line."

The full-lined curve in this figure, marked "N," shows the effect of tension upon the responses. The responses suffered a diminution that was at first rapid in rate and then became progressively slower as the tension was increased from zero up to sixty-one grams.

It will be noted that the base line is rather irregular, though the tension curve is fairly smooth. This condition was found repeatedly, for various tones and intensities. Evidently the procedure was such as to cause variations which involved the base line more than the tension curve. Our opinion is that these variations arose from reflex contractions of the tensor tympani muscle, elicited when the sudden

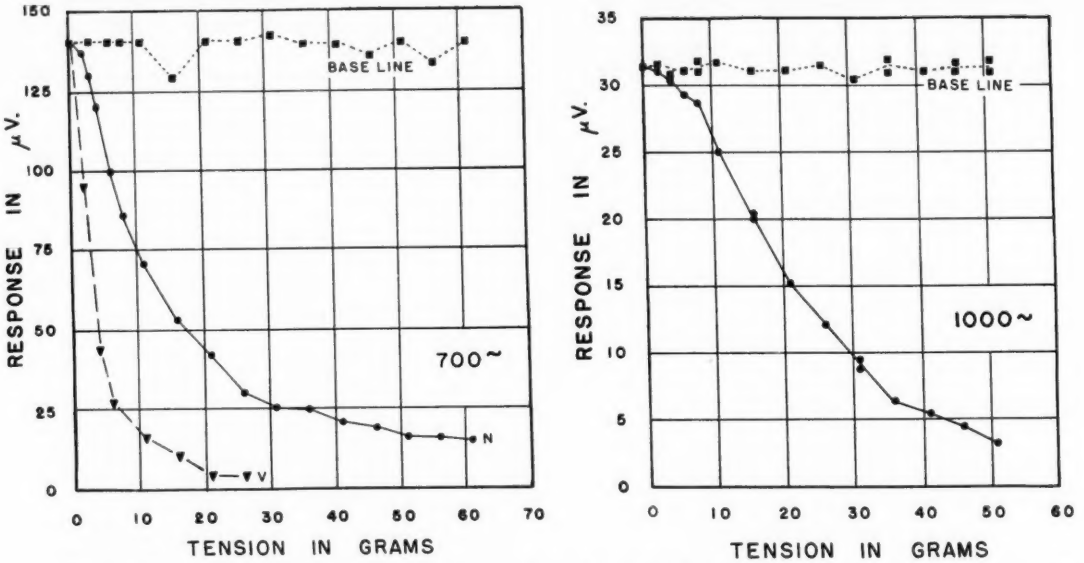


Fig. 1. The effects of tension on the tensor tympani tendon on the electrical responses of the cochlea. Curve *N* is for tension in the normal direction, curve *V* for tension in the ventral direction. The dotted curve is the base line for curve *N*; all the readings were for zero tension, but they are plotted against the abscissa scale to show the order in which they were made. The stimulus was a 700~ tone at an intensity of 10 bars. Animal No. 11.

Fig. 2. Tension curve for 1000~ at an intensity of 1 bar, with normal direction of pull, in an animal in which the fifth nerve had been sectioned. The base line shows the readings for zero tension as in Fig. 1. Animal No. 13.

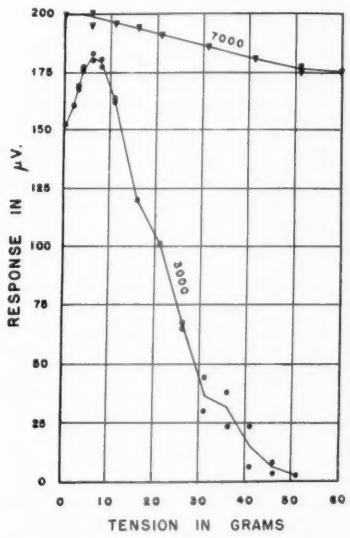


Fig. 3. Tension curves of unusual form due to the presence of overloading. Animal No. 12.

release of tension allowed transmission of the sound at its full intensity.

The dash-lined curve of Fig. 1, marked "V," shows results obtained by pulling directly on the tendon without the glass-tube pulley, after the manner of Crowe and Hughson. It will be seen that the results are qualitatively similar, but that they differ in degree. Tension exerted in the ventral direction is considerably more effective in reducing the responses than tension in the normal direction. The difference between the results of the two methods was much greater for higher frequencies.

In two animals, the tensor tympani muscle was denervated by cutting the mandibular branch of the fifth cranial nerve. After this operation, the base line obtained by the above procedure was very regular. Fig. 2 shows some of the results. The stimulating tone was 1000~ at an intensity of one bar. The tension curve does not differ in any essential respect from that shown in the previous figure.

With particular tones the effect of tension was studied for various intensities of stimulation. It was found that the tension curves are

of the same form for all except the very high intensities of stimulation. For the extreme intensities, which produce overloading of the ear under normal conditions, the tension curves show curious alterations of form. Two curves of this sort are given in Fig. 3. The forms assumed by these curves become understandable only through a consideration of the complete functional relations between response and stimulus intensity.

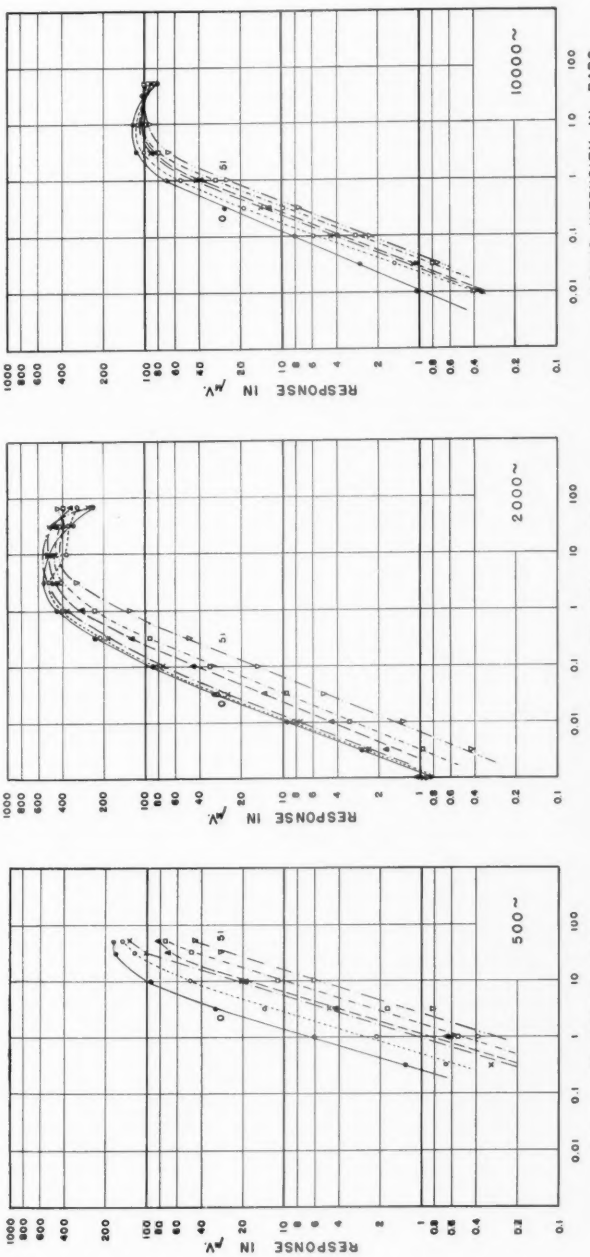
Complete intensity functions were worked out for ten tones between 300 and 10,000~ for animal No. 15. For each frequency, measurements were made of the magnitude of cochlear response for various intensities of stimulation up to the maximum available, first under normal conditions of no tension, and then for tensions of 6, 11, 21, 31, and 51 grams. The functions for three of these tones, 500, 2,000, and 10,000~, are shown in Figs. 4-6.

In these figures, the stimulus intensity in bars of pressure is shown on the abscissa, and the magnitude of response in microvolts on the ordinate. Both scales are logarithmic. The curves as they appear in order from left to right are for zero, 6, 11, 21, 31 and 51 grams of tension; only the first and last are marked.

In Figs. 5 and 6 the curves on the left, marked "0," are typical intensity functions for the cat.[14] They are straight at their lower and middle portions, which on double-logarithmic coördinates indicates a power function. But at high intensities they depart from a power function, attain a maximum and bend downward. For the extreme intensities, therefore, an increase of stimulus intensity causes a diminution of response, and, contrariwise, a decrease of intensity, within limits, causes an augmentation of response. In Fig. 4 the stimulus intensity was not sufficient to give the high degree of overloading shown in the two following figures.

In Figs. 4-6 it will be observed that the curves for various tensions run nearly parallel to the normal curves throughout most of their course. Thus the effect of tension within this range seems to be mainly to shift the curves downward without changing their form or slope. Some of the curves show slight alterations of slope, but the general picture is as described. The effect of tension, therefore, is equivalent to a reduction in sensitivity. The amount of reduction varies for different tones. In Figs. 4-6 it is about 27 db. at 500~, 15 db. at 2000~, and 11 db. at 10,000~, for a tension of 51 grams.

This simple shifting of the tension curves does not continue to obtain for high intensities of stimulation. In general, the greater the tension the higher the stimulus intensity for which the curve remains



Figs. 4, 5, 6. Intensity functions for 500, 2000, and 10,000 — under normal conditions and for various degrees of tension. The curves from left to right are for zero, 6, 11, 21, 31, and 51 grams of tension. Animal No. 15. Fifth nerve cut.

straight, and the less the amount of bending. Within the region of overloading a family of tension curves may show a general crossing, as in Figs. 5 and 6. Beyond the crossings the typical relation between tension and magnitude of response is generally reversed: the response becomes greater when the tension is increased. These features indicate that for strong stimuli the effect of tension is to reduce overloading by reducing the transmission of sound.

These functions explain the types of tension curves shown in the first three figures. Since the functions for different tensions are practically parallel for low and intermediate intensities, it follows that for these intensities the tension curves all have much the same form, like those of Figs. 1 and 2. But if the intensities are sufficient to give overloading, where the functions are no longer parallel, the tension curves will take various forms, as follows:

(1) Within the region before the crossings of the functions, the tension curves will present the usual order of effect, in that greater tensions will give smaller responses. However, the closer the operating point is to the maximum of the functions the less will be the negative slope of the tension curve, as shown for 7000~ in Fig. 3.

(2) If the curves cross practically at one point, as they do in Fig. 6, then for a particular value of sound intensity the effect of tension will be nil. The functions do not always cross at one point, and in such instances the tension curves in the region of crossing will be irregular.

(3) Beyond the crossing point, as already mentioned, the application of tension will increase the responses by reducing the degree of overloading. If the operating point is only a little beyond the crossing, the response curve will rise, attain a maximum, and finally fall as the tension is progressively increased. Such a curve is shown for 3000~ in Fig. 3.

Theoretically, any operating point beyond the crossings should give the form of curve shown for 3000~ in Fig. 3. Actually, this may not happen because there is a limit to the tension that the ossicular system will bear.

The maximum tension that may be exerted upon the tensor tympani tendon without damage to the ear has not been thoroughly investigated. Crowe and Hughson under their conditions used weights up to 50 grams. We have regularly used tensions up to 51 grams, and sometimes up to 61 grams without injury. In one experiment, 76 grams was used successfully until the knot slipped. In

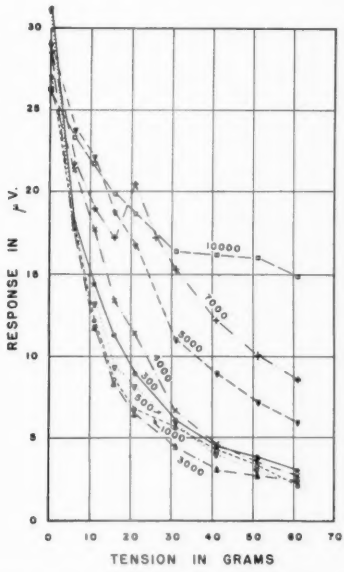


Fig. 7. Tension curves for 8 tones between 300 and 10,000— as indicated. Animal No. 14.

another, 71 grams was used successfully, but 91 grams pulled the tendon loose from its attachment to the bony process of the malleus.

An incidental result of this investigation is to show that experiments that make use of the electrical responses of the ear should regulate and exactly specify the intensity of stimulation, or at least vary the intensity over a sufficiently wide range to determine that the operating point on the intensity function is below the level of overloading. Otherwise the degree of overloading may be such that anomalous results will be obtained: an operative measure or other procedure that ordinarily would be expected to cause an impairment of response may give an improvement, simply because it has resulted in a reduction of overloading.

As some of the above results have already shown, the effects of tension vary as a function of frequency. Fig. 7 shows tension curves for a number of tones, with the stimulus intensity adjusted to give approximately the same amount of response, 30 μv., under normal conditions.

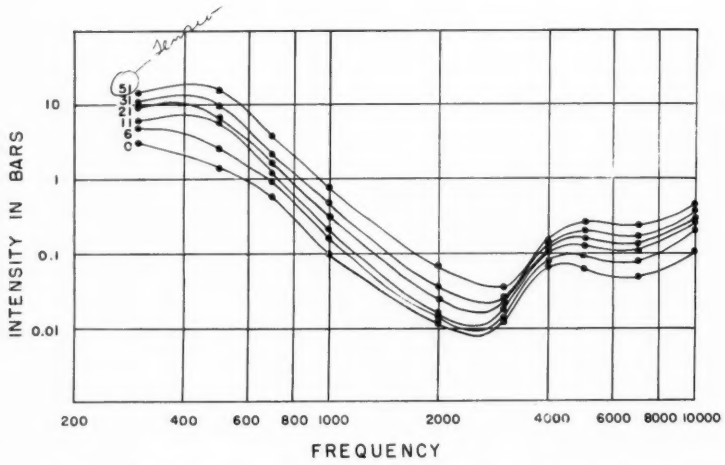


Fig. 8. Equal-response curves for normal conditions and for various degrees of tension. Each curve shows the sound intensity necessary to produce a response of 10 μv. at various frequencies. The numbers to the left of the curves indicate the degree of tension in grams. Animal No. 15. Fifth nerve cut.

Here it may be noted that the curve for 7000~ in this figure shows an unusual variation of form. Such variations have been encountered on several occasions, at levels well below overloading. We have no satisfactory explanation of them, and can suggest only that at specific frequencies and tensions some portion of the transmission system may have been set into resonance.

In this animal, the effects of tension are shown to be somewhat similar for tones between 300 and 3000~, while higher tones are less affected. However, this difference in the effect upon low and high tones should not be taken as an invariable one. The actual relation appears to be more complicated, as further results will show.

The functional relations of tension and frequency are more readily studied when the results are given in the form of equal-response curves, as in Fig. 8. In this figure, each curve shows for a given degree of tension the strength of stimulus necessary to produce a constant magnitude of response of 10 μv., over a wide range of frequencies. Frequency is indicated on the abscissa and sound intensity on the ordinate.

The curves reveal in a clear manner the variation of sensitivity with frequency. For normal conditions of no tension, the maximum sensitivity is between 2000 and 3000~, with a secondary maximum around 7000~.

The most obvious effect of tension is to reduce the sensitivity. This reduction, shown by the raising of the curves, is not equal for all tones, but varies regularly through the frequency scale. It is least around 4000~, and becomes greater for higher tones, and also for lower tones down to 500~, while at 300~ it is less again.

A careful study of this graph gives the impression that the effect of tension is not only to raise the curves, but also to displace them to the right. The normal curve looks as though additional measurements might have given a maximum of sensitivity around 2300 or 2400~, while the 51 gram curve looks as though its maximum might lie fairly close to 3000~, an upward shift of 600 or 700~. An inspection of the curves at other regions bears out this suggestion.

Unfortunately, this type of change in the sensitivity curves was not anticipated, and the procedure was not especially adapted to show it. What obviously is needed is a set of measurements at short intervals of frequency in the region of the normal maximum of sensitivity, or in some other region where the sensitivity is changing rapidly. A further study will be made of this feature. The following discussion is made on the assumption that this suggested result will be verified by additional observations.

Specifically, this assumption is that the application of tension adds both mechanical resistance and stiffness to the ossicular system. The assumption is reasonable on physical grounds, and in fact was first made by Johannes Müller nearly a century ago on the basis of newly discovered principles of vibratory mechanics.[15] Mechanical resistance reduces the amplitude of response of a vibratory system, while stiffness raises the natural frequency.

If the application of tension to the ossicular system not only reduces transmission, but also shifts the sensitivity curve upwards, then the particular relation of tension to frequency will be determined by the form of the sensitivity curve of the ear. Frequencies that lie just below a maximum of sensitivity, or just above a minimum, will be most affected by the application of tension, while frequencies that lie just above a maximum, or just below a minimum, will be least affected. Since the normal sensitivity curves vary somewhat in dif-

ferent cats,[16] the particular relation of frequency and tension in individual animals will vary.

Crowe and Hughson's results are wholly compatible with this hypothesis. The tones that they used, which covered the range 250 to 4000 or 6000~, probably fell within a single broad maximum of sensitivity.

That the normal effect of the tensor tympani muscle is qualitatively like that demonstrated for artificial tensions seems a reasonable assumption. However, the quantitative limitations of this effect are still to be ascertained. We know of no data on the maximum strength of the tensor tympani muscle in the cat. Lorente de Nó[17] measured the contractions of this muscle in the rabbit, and obtained tensions only up to about 1.2 grams. It is likely that the muscle in the cat is considerably stronger.

SUMMARY

The electrical responses of the cochlea were used in an investigation of the function of the tensor tympani muscle. The responses to various tonal stimuli were measured under normal conditions and during the application of artificial tension to the tensor tympani tendon. A thread tied to the tendon was run through a glass-tube pulley placed in the middle ear cavity, and then over a large external pulley to a scale pan. The arrangement made it possible to exert tensions in the normal direction of action of the tensor tympani muscle.

The curves obtained by varying the degree of tension while stimulating with a tone of a given frequency and intensity are of the same general form under most conditions. With increasing tension the responses suffer a diminution that is at first rapid, and then progressively slower.

The tension curves maintain this same form for all except the high intensities of stimulation. For these intensities they show various forms, which are determined by the particular nature of the functional relation between magnitude of response and intensity of stimulation.

These particular relations between intensity and tension are shown most clearly by the determination of intensity functions for normal conditions and for various degrees of tension.

The functional relations of tension and stimulus frequency are complex. Our results are not as complete on this point as is desirable, but they suggest that in addition to its reduction of sound conduction, tension raises the natural frequency of the transmission system

of the ear. These two effects combined give a relation to frequency which is determined by the particular form of the sensitivity curve of the ear.

PRINCETON UNIVERSITY.

REFERENCES

1. Eustachii, Bartholomaei: Opuscula anatomica, Venetiis, pp. 148-164, 1564.

2. Haller, Alberto v.: Elements Physiologiae corporis humani, Tomus Quintus: Sensus externi interni, Lausannae, pp. 282 ff., 1763; Savart, F.: Sur les Usages de la Membrane du Tympan et de l'Oreille Externe. Ann. de chim., 2. ser., 26:33 f., 1824.

3. Henle, J.: Handbuch der systematischen Anatomie des Menschen, Bd. 2: 748, 1866.

4. Mach, E.: Zur Theorie des Gehörorgans. Sitzungsber. d. k. Akad. Wiss., Wien, Math.-Nat. Cl., Abt. 2, 48:283-300, 1863.

5. Magnus, A.: Beiträge zur Anatomie des mittleren Ohres. Arch. f. path. Anat. u. Physiol., 20:79-132, 1861.

6. Pollak, J.: Ueber die Function des Musculus tensor tympani. Medez. Jahrb. 82:555-582, 1886; Kato, T.: Zur Physiologie der Binnenmuskeln des Ohres. Arch. f. d. ges. Physiol., 150:569-625, 1913.

7. Cf. Hallpike, C. S.: On the Function of the Tympanic Muscles. J. Laryngol. and Otol., 50:362-369, 1935; Wever, E. G., and Bray, C. W.: The Nature of Acoustic Response: the Relation between Sound Intensity and the Magnitude of Responses in the Cochlea. J. Exper. Psychol., 19:131, 1936.

8. Politzer, A.: Untersuchungen über Schallfortpflanzung und Schallleitung im Gehörorgane im gesunden und kranken Zustande. Arch. f. Ohrenh., 1:59-73, 1864.

9. Lucae, A.: Untersuchungen über die sogenannte "Knochenleitung" und deren Verhältniss zur Schallfortpflanzung durch die Luft, im gesunden und kranken Zustande. Arch. f. Ohrenhk., 1:303-317, 1864.

10. Mach, E., and Kessel, J.: Versuche über die Accommodation des Ohres. Sitzungsber. d. k. Akad. Wiss., Wien, Math.-Nat. Cl., 65:337-343, 1872.

11. Crowe, S. J., and Hughson, W.: Eine neue Methode zur Untersuchung der Physiologie und Pathologie des Ohres. Zsch. f. Hals...hk., 30:71-72, 1931; Crowe, S. J., Hughson, W., and Witting, E. G.: Function of the Tensor Tympani Muscle. Arch. of Otolaryngol., 14:575-580, 1931; Hughson, W., and Crowe, S. J.: Experimental Investigation of the Physiology of the Ear. Acta Oto-laryngol., 18:305-307, 1933.

12. Heidenhain, R.: Ueber secretorische und trophische Drüsennerven. Arch. f. d. ges. Physiol., 17:16-17, 1878.

13. Wever, E. G., and Bray, C. W.: The Nature of Acoustic Response, etc. J. Exper. Psychol., 19:130 f., 1936.

14. Wever, E. G., and Bray, C. W.: The Nature of Acoustic Response: the Relation between Stimulus Intensity and the Magnitude of Cochlear Responses in the Cat. To appear in J. Exper. Psychol. for Jan., 1938.

15. Müller, J.: Elements of Physiology. Trans. by W. Baly. Vol. 2, 1256-1264, 1843.

16. Wever and Bray: See work cited in Reference 14.

17. Lorente de Nó, R.: The Reflex Contractions of the Muscles of the Middle Ear as a Hearing Test in Experimental Animals. Trans. Amer. Laryngol., Rhinol., and Otol. Soc., 1933.

LXXVIII

X-RAY VISUALIZATION OF THE NASO-LACRIMAL DUCT*

GEORGE E. HOURN, M.D.

ST. LOUIS

A few years ago during a casual study of the naso-lacrimal fossa and canal in the skull, it occurred to the writer that it might be advantageous in some pathological conditions to use a modified dental x-ray film within the nasal chamber. By this procedure one might eliminate the confusing interposed bone shadows such as one encounters in the usual lateral view after injection of radiopaque material into the efferent naso-lacrimal apparatus. By so doing, one can procure a more detailed and intimate picture of the naso-lacrimal duct in health and disease.

However, this method does not supersede nor displace the usual antero-posterior and lateral plates after radiopaque injections, but serves where indicated as a supplementary aid in a more thorough study of this region.

The use of radiopaque material as an adjunct to the x-ray study of the lacrimal apparatus is not confined to the last decade or two, but was used as early as 1909 by the late Dr. A. E. Ewing[1] of St. Louis, in an investigation, to use his own words, of the "size and shape of the lacrimal abscess with the hope that some knowledge of its hidden recesses might be obtained which would aid in its more skillful management."

Later, Von Szilly, Campbell, Carter and Daub, Castresana, Ploman and others have stressed, with more or less enthusiasm, the value of x-ray visualization of the naso-lacrimal duct using radiopaque material.

It is quite evident that a more accurate conception of the normal or pathological sac or duct can be obtained by this means than by any other method at our disposal. In a preliminary study of treatment or prospective operative interference, in disorders peculiar to the efferent lacrimal apparatus, it is of definite value to have a clear picture of the exact point of stricture, whether in the canaliculi,

*Presented before the Fifty-ninth Annual Congress of the American Laryngological Association, Atlantic City, June 2, 1937.

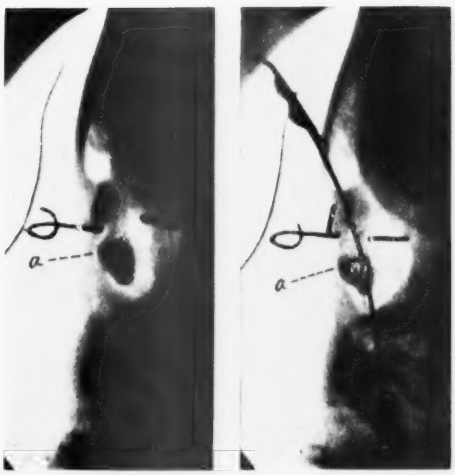


Fig. 1. An x-ray taken in 1909 after injection of lacrimal sac with bismuth paste by Dr. A. E. Ewing.

lower part of the sac, in the duct or at the nasal ostium. Information as to the size and shape of the sac, whether ectatic or contracted, as to the presence of diverticula, irregularities, side to side union of sac and duct, and various other anomalies can be obtained. Thus the treatment or operation best adapted to the abnormal condition present can be more effective. The visualization, it seems, would be of distinct value preliminary to dacryocystorhinostomy and also to check the results as suggested by Campbell, Carter and Daub.[6] In the combined operation such as the Mosher-Toti, or intranasal sac operation, one has to consider the probable anterior ethmoid cell or cells in relation to the floor of the lacrimal fossa so clearly stressed by Mosher[3] and Whitnall.[4] By using the Proetz[5] displacement method with lipiodol to visualize the anterior ethmoid cells, an intranasal film may be of value in revealing this relationship. Campbell and associates suggest using a bismuth stripe over the ventral extremity of the middle turbinate to determine the anterior overhang of this turbinate in its relation to the lacrimal fossa.

At this point it might be well to discuss very briefly the anatomical factors entering into a proper interpretation of the films resulting from the methods under discussion in this paper.

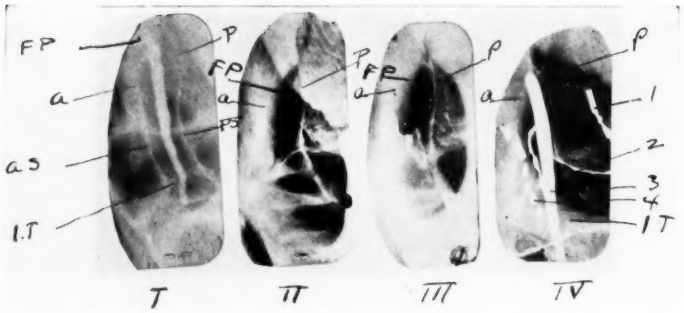


Fig. 2. No. I. Injected normal lacrimal sac and duct. No. II, III and IV are x-rays of lacrimal fossa and duct in skull.

a, ant. crest: p, post. crest: a. s., ant. lip of sulcus: p. s., post. lip of sulcus: i. t., inf. turb.: f. p., front. process:

In No. IV lead markers are placed in lacrimal canal and fossa (3); over anterior tip of middle turbinate (2); over uncinate process (1); over infra orbital margin (4).

Three osseous structures enter into the formation of the lacrimal fossa and canal, namely, the superior maxillary, lacrimal and inferior turbinate bones.

In the first named, the dense frontal process is bounded posteriorly by the lacrimal sulcus, having more or less marked anterior and posterior lips which diverge inferiorly where the sulcus merges into the cupola of the inferior meatus. The upper portion of this sulcus forms the anterior dense floor of the lacrimal fossa, while the posterior portion of the floor is made up of the thin fragile lacrimal bone. The lacrimal fossa is bounded anteriorly and posteriorly by crests, the anterior one less defined above, while the more prominent posterior crest is prolonged anteriorly in its lower portion by the hamular process so as to define the lateral orbital opening of the lacrimal canal. Medially, the lacrimal bone bridges over the upper portion of the lacrimal sulcus and the inferior turbinate bridges over the remaining portion of the sulcus by means of its lacrimal process, so as to convert it into the lacrimal canal. Thus, the nasal opening, because of its divergent walls, is shaped more or less like an inverted funnel, while the orbital opening has a sharply defined lateral margin.

Fig. 3. Radiograph (by J. D. Morgan) showing relation of lacrimal sac and duct to the lateral wall of the nose. (From Whitnall's "Anatomy of the Orbit.")

In the intranasal film, the crests of the lacrimal fossa, the diverging lips of the lacrimal sulcus and the bridging over of the inferior turbinate is visible in the average case. However, when one encounters a shallow fossa where the crests are not so prominent or where the frontal process makes up in a large part the fossa, the landmarks may not be so conspicuous. To some extent, the part occupied by the dense frontal process in the formation of the fossa can be visualized.

As mentioned above, Mosher and Whitnall have stressed the presence of anterior ethmoid cells medial to the upper portion of the lacrimal fossa. The latter states that in one hundred skulls, fifty-four per cent extended to anterior lacrimal crest and even into the frontal process, thirty-two per cent to the lacrimo-maxillary suture and fourteen per cent to the posterior lacrimal crest. These cells can be located by Proetz displacement method and intranasal film, as previously mentioned.

In the deeper relation, Thorsch found in seventy-nine skulls, the middle turbinate covered the fossa in fourteen, partly in thirteen and posterior to the fossa in fifty-two cases. This relationship can be determined by using some radiopaque material over the anterior end of the middle turbinate as suggested above.

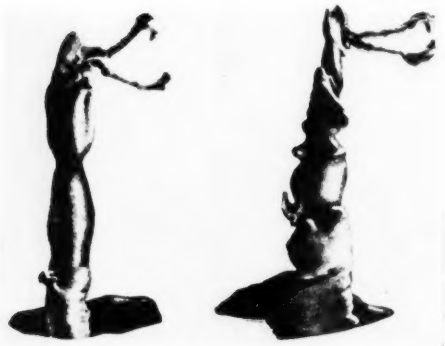


Fig. 4. Regular and irregular types of the membranous naso-lacrimal passages. (From J. Parsons Schaeffer.)

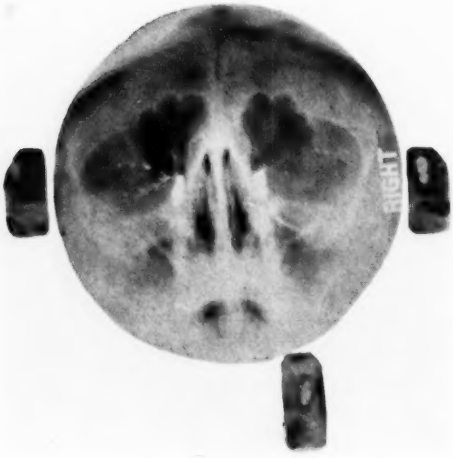


Fig. 5. The central film is in the Water's position and reveals a bilateral stenosis with dilated sacs. On either side are the respective nasal films. The lower nasal film shows an anterior ethmoid cell in relation to the lacrimal fossa. This cell was filled by the Proetz method. The lacrimal sac was not injected with lipiodol in this radiograph.

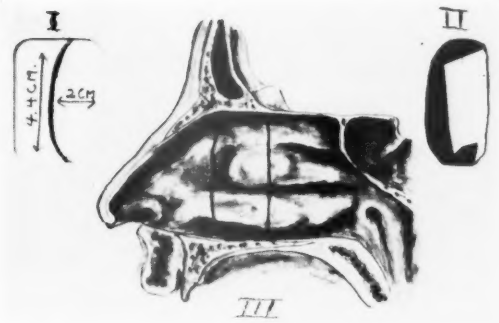


Fig. 6. "II," nasal film made from dental film as in "I." Film placed in nasal cavity as in "III."

Anatomically, the membranous lacrimal sac and lacrimal canal is made up of the orbital, maxillary and meatal portions. The first named comprising the lacrimal sac is not normally a clearly defined sac but is a continuation of the lacrimal duct without a sharp line of demarcation. Into the lateral part of the sac, a little above its mid portion and beneath the internal palpebral ligament, the inferior and superior canaliculi open usually by a common duct. The vertical and horizontal portions of the canaliculi are occasionally well defined in the x-ray of an injected case. The maxillary portion of the duct is that part in relation to the superior maxilla below the superior opening of the lacrimal canal and the meatal portion is that part in relation to the inferior meatus and is of variable length due to the variation of the location of its nasal ostium in the lateral wall of this meatus.

J. Parsons Schaeffer[6] and others have demonstrated many variants from the so-called typical naso-lacrimal duct. He succinctly states the facts as follows:[7] "The idea of an unvarying typical type of adult naso-lacrimal duct and lacrimal sac must be abandoned. The newer anatomy of anatomic types is urged. This is more in keeping with the real anatomy than the notion of a typical form, and all departures therefrom are anomalies. Recent investigations show at least two important types of naso-lacrimal ducts are encountered. One type is more or less regular in contour and in direct line with the lacrimal sac with which it gradually merges. The other type is

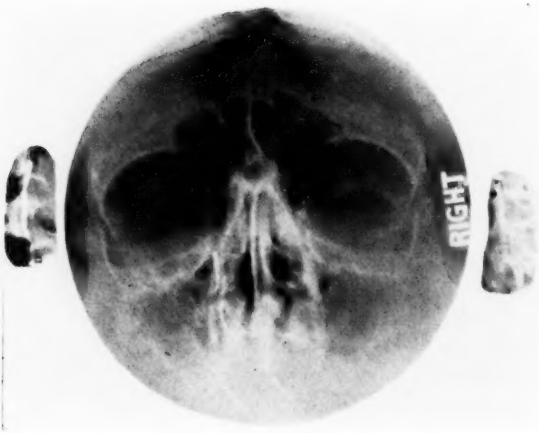


Fig. 7. Note normal duct on the left. On the right no lipiodol entered the sac. Constriction apparently at the common duct.

Eight to ten minutes after injection, the left duct partially emptied as shown in antero-posterior view.

very irregular, somewhat tortuous and not infrequently connected with the lacrimal sac in a side to side union. Both types of ducts may have diverticula of various sizes. However, diverticula are more frequently encountered in ducts with irregular walls." A number of observers have described so-called valves, notably at the junction of the sac and duct and at the nasal ostium or between these two locations. These are most probably mucosal folds resulting from embryological remnants. By means of x-ray visualization when these passageways are filled with radiopaque material, a fairly accurate picture may be obtained of the membranous duct and sac. For this purpose an antero-posterior view in the Water's position should be taken as well as the lateral view. If x-rays were utilized before probing there would be fewer false passages.

For a satisfactory visualization of the naso-lacrimal duct one should have an antero-posterior view as well as a lateral view for obvious reasons. The intranasal film, as a substitute for the lateral view, is reserved for adults which do not present the technical difficulties such as one would encounter in children and infants, or in

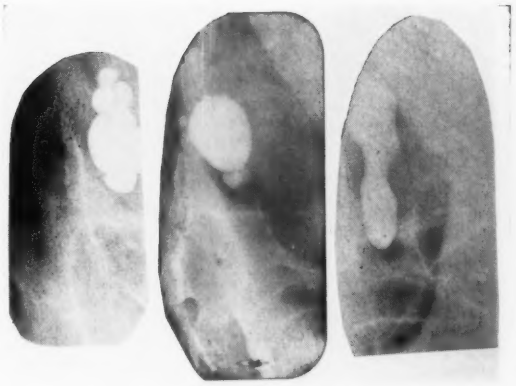


Fig. 8. Stenosis at lower portion of sac in the first two radiographs, while in the third the stenosis is in the middle third of the duct.

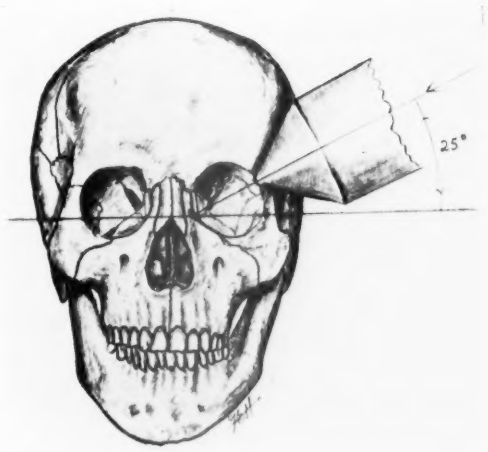


Fig. 9. Position and angulation of x-ray tube in making exposure.

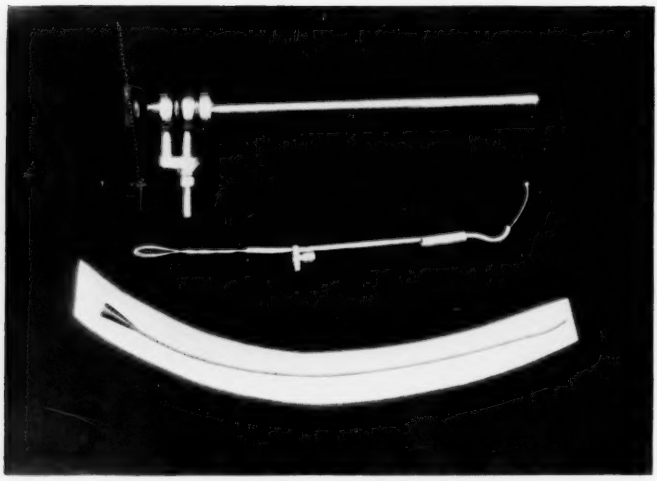


Fig. 10. Antroscope, naso-lacrimal ostia director with probe, and No. 4 silk wound catheter.

adults where abnormal conditions are present in the nose interfering with the proper placing of the film within the nasal chamber.

I have found the Eastman dental radiotized film, when cut down, quite satisfactory. This makes a pack 2 cm. in width, 4.4 cm. in length and 1 mm. in thickness. After the nasal chamber has been cocainized and the turbinates shrunken with epinephrin, the average adult nose will accommodate the pack. Since the plane of the film can be altered to suit the conditions present, one can usually pass the frequent septal deviations, although it may be necessary to push the middle turbinate towards the lateral wall. If one encounters an insurmountable obstruction, the other nasal chamber can be utilized. Needless to say, the patient appreciates gentle manipulation at this phase of the procedure. When the pack is in correct position, the anterior border should extend at least 5 mm. anterior to the ventral extremity of the middle turbinate and the base of the film should be over the second bicuspid to the second molar teeth, so that the axis of the film covers approximately the junction of the anterior and middle thirds of the inferior turbinate.

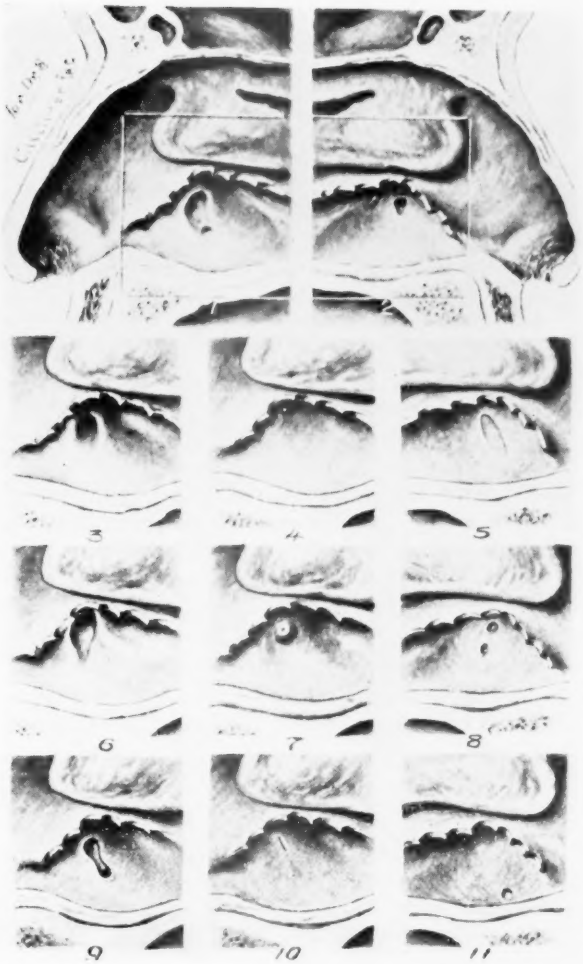


Fig. 11. Variations in location and shape of the naso-lacrimal ostia. (J. Parsons Schaeffer.) Drawings of actual dissections illustrating various types of ostia nasolacrimalia encountered in this study. The reader is referred to the text for a further consideration of them. The concha nasalis inferior is partly cut away so as to expose for study the manner of communication between the ductus nasolacrimalis and the meatus nasi inferior.

I have been using lipiodol diluted with equal parts of olive oil for the pathological cases with stricture or partial obstruction, and the more viscous unaltered lipiodol for the normal lacrimal duct and in those passageways which empty more or less promptly. It is especially important in the latter group of cases to inject the radiopaque material in the x-ray room and be prepared for prompt exposure to insure the lipiodol being in the lacrimal duct at the time of taking the picture. Ordinarily the injection of the lacrimal passageways is readily accomplished after preliminary cocainization of the conjunctival sac via the inferior or superior canaliculus through the normal or dilated punctum. The contents of the lacrimal sac should be expressed before injecting. I am using a number 24 needle whose calibre offers considerable resistance to the unaltered lipiodol, yet this objection is outweighed by the facility with which it can be introduced into the punctum.

The technique of the x-ray exposure is most important in producing a satisfactory picture. The central ray of the x-ray tube should pass slightly anterior to the dense superior lateral portion of the superior orbital margin near the zygomatico-frontal suture, medially and caudally, at an angle of twenty-five degrees to the lower end of the lacrimal fossa. By this angulation, the dense superior orbital and the compact inferior orbital margins will not project their objectionable shadows on the lacrimal duct so as to blot out the desired details of the picture. To facilitate an accurate angulation and position of the tube, the Dental Pointer Cone, which is extensively used in dental radiology, is invaluable. An exposure of two seconds on Eastman radiotized film (using sixty kilovolts and twenty-five milliamperes at a target-film distance of eighteen inches) is approximately correct.

In stricture of the lacrimal duct, one can easily determine by the above-described methods the condition of the duct above the stricture. One's curiosity is aroused as to the condition of the duct distal to the stricture. To satisfy that curiosity, I recently had Mr. C. R. Storz of St. Louis make up a tube curved at the end so that a No. 4 silk wound catheter would be directed upwards at approximately ninety degrees. This is attached to clasps which can be slipped over an antroscope, so that one can direct the catheter by direct vision into the nasal ostium of the lacrimal duct. It is obvious that this procedure will encounter serious obstacles in a narrow nasal chamber or in a marked low deviation of the septum. Through this same director one can also probe the lacrimal duct in favorable cases from below. For this purpose, Mr. Storz soldered a

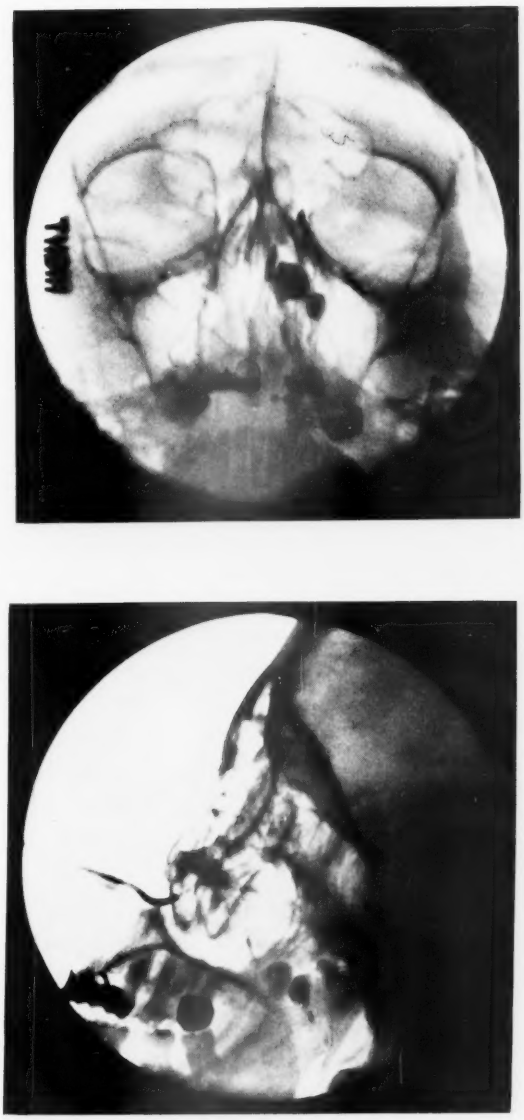


Fig. 12. Lipiodol injection of lacrimal sac and duct via the nasal ostium.

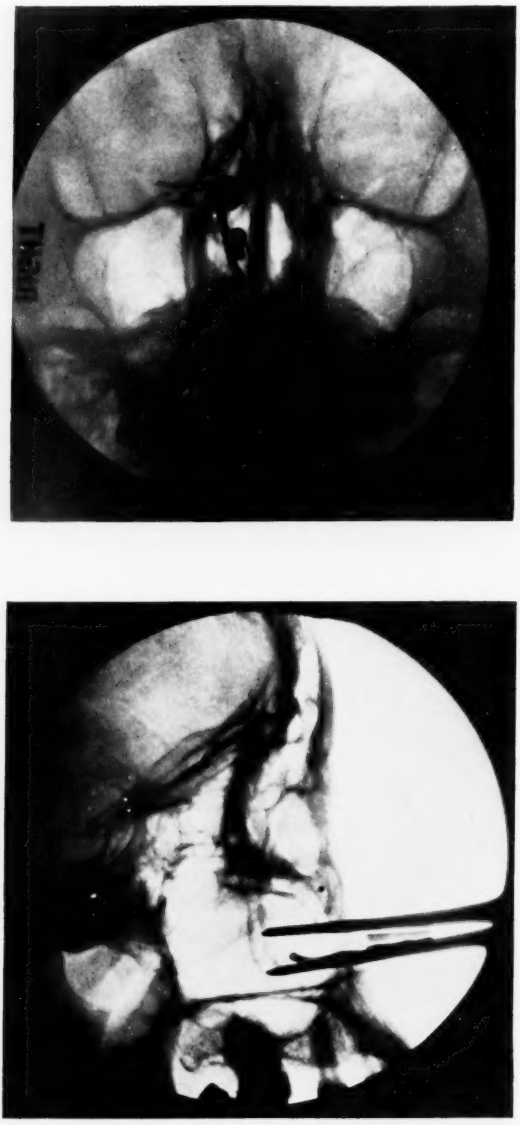


Fig. 13. Probe introduced into the lacrimal duct by way of the nasal ostium.

ball (about 15-gauge) onto the tip of a No. 31 flexible shaft of piano wire.

Since the nasal ostium presents such a variation in location, shape and size, there may be considerable difficulty in identifying it. The patent openings as in No. 1, No. 3, No. 6 or No. 9 are easily located, but the identification of the slit or punctate ostium is apt to prove exasperating in the presence of mucus. A long self-retaining speculum that will displace the anterior portion of the inferior turbinate medially and upwards, is quite essential in the procedure.

As in retrograde bouginage in stenosis of the larynx and esophagus, I suspect there may be some value in probing an occasional stenotic lacrimal duct from below, but, unfortunately I have not had the time or opportunity to use it on a pathological case since this nasal ostium director has been made. However, I have used it on a couple of normal patients and present a lipiodol x-ray visualization of the lacrimal duct, injected via the nasal ostium and a second x-ray showing a probe in the lacrimal duct, inserted by way of the nasal ostium.

In conclusion, I realize there are technical difficulties and obstacles that may make impractical the universal use of the intranasal film and use of the nasal ostium for injection and probing of the lacrimal duct, but I hope it may be of useful service where indicated.

UNIVERSITY CLUB BLDG.

BIBLIOGRAPHY

1. Ewing, A. E.: Roentgen Ray Demonstrations of the Lacrimal Abscess Cavity. Amer. J. of Opth., 24:1-4.

2. Campbell, Carter and Daub. Roentgen Ray Studies of the Naso-lacrimal Passageways. Arch. of Opth., 462-470, 1922.

3. Mosher, H. P.: Re-establishing Intranasal Drainage of the Lachrymal Sac. Laryngoscope, 31:492-521, 1921.

4. Whitnall, S. E.: Anatomy of the Human Orbit. p. 68.

5. Proetz, A. W.: The Displacement Method of Sinus Diagnosis and Treatment. Annals Publishing Co., St. Louis, Mo. 1931.

6. Schaeffer, J. Parsons: The Nose and Olfactory Organ. Chapter 7. P. Blakiston's Son and Co., Philadelphia, Pa. 1920.

7. Schaeffer, J. Parsons: The Modern Conception of the Anatomy of the Naso-lacrimal Passageways in Man. Amer. J. of Opth., p. 683, 1921.

LXXIX

THE WEVER AND BRAY PHENOMENON—A SUMMARY OF THE DATA CONCERNING THE ORIGIN OF THE COCHLEAR EFFECT

C. S. HALLPIKE*

AND

A. F. RAWDON-SMITH†

INTRODUCTION

Since Wever and Bray's original discovery in 1930 of the phenomenon which bears their name a considerable body of literature has arisen on the electrophysiology of the ear. The present paper is primarily concerned with summarizing such of this as is relevant to the origin of that component of the phenomenon which is now known as the "cochlear effect." In order to permit this it will be necessary first to discuss the evidence which has led to the present clear distinction between this effect and the somewhat similar phenomenon detectable in the eighth nerve due to the passage of syncronized nerve impulses. To this end, therefore, it is first proposed to summarize Wever and Bray's original papers, and to examine their conclusions in the critical light of the later experimental analysis to which they have been subjected. The second section of this work will be devoted to a discussion of the later hypotheses of origin of the effect.

WEVER AND BRAY'S ORIGINAL WORK, AND THEIR CONCLUSIONS

The apparatus used by Wever and Bray in their classic experiments[31 32] was arranged in the following way: The amplifier, telephone receivers and the observer were installed in a sound-proof room. The cat was arranged external to this, with the recording electrode inserted intracranially onto the eighth nerve. Listening at the telephones, the observer was able to understand words spoken into the animal's ear, and even to recognize the speaker by his voice. It was evident, therefore that the reproduction, in the form of electrical potential variations, of the major frequencies of the speech spectrum was sensibly linear—little more distortion than occurs in a commer-

*From the Ferens Institute of Otology, Middlesex Hospital, London.
†From the Psychological Laboratory, Cambridge.

cial telephone can have been present. As to the origin of the effect, Wever and Bray were able to satisfy themselves that it was a vital one, in that it was dependent upon the functional integrity of the cochlea. They mentioned the possibility that the electrical effect may have been produced within the cochlea, in a manner not specified. But they preferred to consider the potential variations as due to action currents in the eighth nerve for the following reasons:

(1) The potentials were of greater amplitude when the active electrode was in the brain stem than when it was at any other point equidistant from the cochlea; the lines of nervous conduction were thus followed; and

(2) With an electrode on the brain stem, and the return electrode somewhere distant from this point (the opposite cochlea having been destroyed), the effect was removed by section of the auditory nerve of the ear stimulated, even though the intervening space was filled with some electrical conducting medium such as saline solution.

With regard to the first of these points, it must be stated that this finding has never been confirmed. Adrian[1] was the first to point out that the effect was by no means confined to the eighth nerve, and that the *fenestra rotunda* gave a particularly large response. Davis and his co-workers[10] confirmed this, and noted also that the *subarcuate fossa* gave a good response. Adrian suggested *(loc cit.)* that the large response at the round window would be explicable if it were assumed that the cochlea were acting as a microphone, translating the air pressure variations constituting the stimulus into variations of electrical pressure, the suggestion originally rejected by Wever and Bray themselves,[30,31] for then the round window membrane would constitute a path of low electrical resistance from the cochlea fluids to the active electrode. For Adrian assumed, rightly, that the bony wall of the cochlea would behave as an electrical insulator. This explanation of the large size of the potentials at the round window membrane received support by the discovery by Hallpike and Rawdon-Smith[18] that potentials of comparable size could be obtained from an electrode inserted into a mercury filled hole bored in the bony cochlear wall in such a way as to reduce the electrical resistance, whilst not causing mechanical damage to the cochlear elements. A brief description of their technique may be given here.

The mucous membrane over the bony cochlea is first reflected, and, using a fine dental drill, a small hole is made in the bony wall. This operation is carried out under inspection through a dissecting microscope. The bone is dense and avascular, and often several milli-

metres in thickness. Both these properties are in complete accordance with the view that it would constitute an adequate insulating medium for the electrical potentials generated within. The floor of the small concavity formed by this method may, with practice, be reduced to a very small thickness; a thickness of so small an order, indeed, that a slight wetness of the floor may be recognized through the microscope, due to the outward passage of minute quantities of endolymph or perilymph through the remaining bone. At this stage the concavity is filled by means of a micropipette with a small mercury bead, which serves the dual purpose of preventing any further fluid escaping, and establishing low-resistance electrical contact with the interior of the cochlea.

The fact that electrical potentials as great as those obtained from the auditory nerve could be obtained from a fine platinum electrode inserted into the mercury-filled holes just described, justifies the rejection of Wever and Bray's supposition that the potentials which they had found were wholly due to the presence of nervous impulses, on these grounds alone. It is none the less necessary to attempt an explanation of their second finding, namely, that section of the acoustic nerve caused cessation of the effect. Adrian[2] tentatively suggested that this abolition of the effect was due not directly to section of the nerve, but to the concomitant severance of the vascular supply to the internal ear. The artery supplying this lies in a well-defined connective tissue bundle, anterior to the nerve and in intimate contact with it. Section of the nerve without section of the artery was successfully accomplished by the authors[18] and, under these conditions, the response from the central end of the cut nerve persisted almost without reduction, but disappeared in a few seconds after division of the vascular strand.

With the completion of this experiment, both Wever and Bray's two major reasons for supposing a neural origin for the Wever and Bray effect disappeared. The phenomenon was generally held to be a microphonic one,[1 2 18] the origin of which was not precisely known. Closer study of the electrical phenomena of audition in the cat later revealed, however, that true action potentials could be detected in the eighth nerve, provided that the spurious potentials due to the Wever and Bray effect were removed, either by the employment of small co-axial electrodes, or by recording from such parts of the brain stem as were sufficiently distant from the cochlea to prevent electrical spread of the potentials generated within.[10] It thus became necessary to distinguish two sorts of response in the eighth nerve, namely, that which Davis[7 10] calls the "cochlear component," a term used to designate the effect having its origin within the coch-

lea, and true action potentials in the eighth nerve. It is convenient to discuss the major differences between these two effects under the following headings:

(1) *Masking of One Stimulus by Another.*—If two sounds are simultaneously delivered to the ear of an animal, the cochlear response and the nerve response behave quite differently. In an oscillogram of the former, both stimulating patterns may be recognized summing with one another, in a manner such as would be found were an oscillogram of a microphone to be examined in the same way.[7,10] In the case of the action potentials, however, the responses may exhibit mutual interference; the phase relationship of the two stimuli employed is of primary importance in determining which of the two responses will be masked, but in all cases the total response is very different from that at the round window.

(2) *Resistance to Cold, etc.*—The cochlear response is much more resistant to cold,[3] general anaesthesia,[7] death of the animal[18] and lack of blood supply[7] than are the action potentials.

(3) *Polarity.*—"If the polarity of the stimulating wave-train is reversed, the polarity of the cochlear response is also reversed, whereas the nervous component retains its characteristic polarity and form."[7]

(4) *Wave-Form.*—The wave-form of the cochlear response is markedly different from that of the action potential response. The former reproduces with remarkable fidelity the wave-form of the incoming sound stimulus;[18] indeed, the accurate reproduction of a sinusoidal stimulus, both in wave-form and in serial uniformity, is such as almost to preclude any question of the neural origin of the effect, on this count alone. The wave-form of the neural effect is, as would be expected, a series of sharp transients, the form and polarity of which are characteristic of all action potentials.

(5) *Latent Period of the Two Responses.*—The cochlear component appears extremely shortly after the arrival of a wave at the tympanic membrane. The short interval found is probably due to the time taken for the vibration to traverse the vibrating components of the middle ear to the round window membrane. The latencies found are of the order of .0001 sec.[7] The neural component has a much longer latent period, the exact length being dependent upon the site of the recording electrodes, as would be expected. At the round window the latency is approximately .0007 sec., whilst in the contralateral auditory tracts of the mid-brain it may be as long as .002 sec. At intermediate positions, it lies between these limits.

From this evidence, there is no doubt that the cochlear effect and the action potential are distinct phenomena. It is now convenient to summarize the various theories which have been held as to the probable origin of the cochlear phenomenon, before proceeding to their critical examination.

The Neural Hypothesis.—It is clear from the foregoing discussion that to postulate that the potentials have their origin in the trunk of the eighth nerve is no longer possible. This does not, however, exclude the possibility of a neural origin, for it has been suggested that the potentials arise in the terminal fibres of the auditory nerve, within the cochlea (Hallpike and Rawdon-Smith, 1934b); in the ensuing discussion this possibility will be referred to as the neural hypothesis of origin.

Non-Neural Hypotheses. (a) *The "fluid microphone" suggestion.* This suggestion was originally put forward, in this connection, by Adrian,[1] though a comparable suggestion had been made by Helmholtz to account for certain similar although non-vital phenomena; Helmholtz's suggestion was later quoted in connection with the Wever and Bray effect by Leiri.[21] Briefly, the suggestion is that, as when certain solutions are compressed, potential differences of a small order may be measured across their length, so in the cochlea it is the compression of the endolymph and perilymph fluids themselves which gives rise to the Wever and Bray potentials.

(b) *The "sensory cell" hypothesis.* This theory was put forward originally by Davis and his co-workers in 1934.[10] It states, to quote from Davis:[7]

"The mechanical vibration causes the sensory cells of the organ of Corti to develop an electrical potential between their upper and lower ends. The energy for this electrical potential is derived from the sound waves. Whether this cochlear response is part of the mechanism for the excitation of nerve impulses or whether it has no physiological significance is still uncertain * * *."

(c) *The Membrane Hypothesis.* Non-neural hypotheses include, lastly, the membrane hypothesis,[18] according to which the potential changes are conceived as being engendered by the movements of hypothetical polarized structures within the cochlea; the movements themselves being caused by the pressure changes set up in the fluids of the inner ear by incoming sound vibrations. The polarized structure immediately suggesting itself is the membrane of Reissner, separating the endolymph from the perilymph of the *scala vestibuli*; the theoretical justification for regarding this membrane as polarized

rests upon the fact that the two fluids have different origins, the perilymph being cerebro-spinal fluid, and secreted by the choroid plexuses, whilst the endolymph is secreted within the relatively small and circumscribed endolymph system itself, probably by the *stria vascularis*.[13] The fact that these fluids are of different origins makes it likely that they are of different ionic concentrations (Rossi, 1914), it is therefore not impossible that an intervening membrane, almost certainly semi-permeable, such as that of Reissner, would, in fact, be polarized.

It is now necessary that these four hypotheses of origin of the cochlear effect be examined in the critical light of such experimental evidence as has accumulated since their conception.

(I) *The neural hypothesis in the light of the later experimental evidence.* On the neural hypothesis, as has been said, the cochlear potentials are thought to arise in the terminal fibres of the eighth nerve. The evidence in favor of this view is as follows: It has been pointed out above that, on section of the auditory nerve, with conservation of the blood supply to the cochlea, the Wever and Bray potentials as measured at the round window membrane are unaltered for some hours. Previous to the work about to be described, however, little was known about the later effects upon the electrical response of section of the nerve alone, or of the nerve and artery together. In 1934, however, Guttman and Barrera[11] published the results of an experiment in which the eighth nerve was cut, in a number of cats, sometimes with concomitant section of the close-lying artery, sometimes without. Degeneration of the neural elements of the cochlea followed, as described by Wittmaack;[31] widespread degeneration of the ganglion cells and nerve fibres of the cochlear neurones was found, peripheral to the point of section, after varying intervals from ten days to six weeks which were allowed to elapse between the section of the nerve and the death of the animal. Yet in every case Guttman and Barrera report that there was no reduction in the cochlear electrical response, as measured by listening with a pair of telephones to the amplified potentials engendered by various forms of acoustical stimulation. Before the value of these results can be assessed, it will be necessary to discuss in greater detail the histological results following upon section of the auditory nerve.

Wittmaack's conclusions as to the consequence of this operation in the cat have already been stated. It will be seen at once that the results he reported are in striking opposition to the classical laws of Wallerian degeneration. According to Waller, no degeneration should take place in those fibres still attached to their cell bodies. Yet wide-

spread degeneration of the peripheral neurones distal to the point of section actually occurred. Wittmaack's view, therefore, met with some objection in the later discussion of his work. Siebenmann[28] pointed out that a difficulty arose when any attempt was made to attach a neural significance to these results; the position, according to Siebenmann, was much confused by the disturbance of vascular supply consequent upon the severance of the internal auditory artery, concomitant with section of the nerve in question. Wittmaack,[31] however, defended his views on the grounds that concomitant section of the artery was prevented by the employment of a blunt dissector for the nerve section, the more resilient artery being resistant to such an instrument. He pointed out also that, in strict accord with the Wallerian view, the cells and fibres of the peripheral vestibular neurones showed an almost complete absence of degenerative change. Now the blood supply to both vestibular and cochlear neurones is via the internal auditory artery, and the absence of degenerative change in the former, with considerable alteration in the latter, precludes the possibility that the latter change can be ascribed to section of the artery in question. Latterly Wittmaack's views have received considerable impetus from the work of Crowe[6] and of de Kleyn and Gray[23] upon the histological changes engendered by tumors involving the eighth nerve. Both these papers report changes of a very much greater order in the cochlear than in the vestibular neurones, which bears out Wittmaack's original statement. Further, in the rabbit, Kaida[22] has reported two widely different types of histological result, following upon section of this nerve. Firstly, he describes gross degeneration of all neural cochlear elements, together with alterations in the appearance of the sensory epithelium of the cochlea with collapse of the basilar membrane and the membrane of Reissner, and disappearance of the organ of Corti. Secondly, the vestibular portion of the internal ear exhibited changes of strictly comparable type and severity. Such a histological picture, Kaida correlated with concomitant severance of both auditory artery and eighth nerve. In some animals, however, Kaida demonstrated histological changes more in accord with those described by Wittmaack. In these he found good preservation of the sensory epithelium and membranes, with disappearance of the cells of the spiral ganglion and of the nerve fibres within the modiolus. Kaida's opinion that in these cases the vascular supply had remained intact is adequately supported by the fact of the preservation in an undegenerated state of the fibres of the peripheral vestibular neurones and the cells of Scarpa's ganglion. It must here be pointed out, however, that on one point Wittmaack and Kaida are in poor agreement. Whilst Wittmaack states that, under these conditions, the sensory cells of Corti's organ show some degen-

erative change, Kaida urges that they may present an appearance indistinguishable from normal.

On the basis of these results, it is possible to assess the work of Guttmann and Barrera, which has been previously described. (The major histological findings of the early workers have been substantially corroborated by the work of Hallpike and Rawdon-Smith, to be described later.[19]

Guttmann and Barrera stated that degeneration of the cochlear nerve comparable to that described by Wittmaack might be associated with a normal cochlear response. A difficulty in the interpretation of their finding is raised by their statement that in some of their cases the internal auditory artery was divided. As previously pointed out by the authors, it is a matter of general agreement that interruption of the blood supply to the cochlea leads to a rapid and persistent fall in the cochlear response to the post-mortem level. Histologically this fall is associated with a general necrosis of the cochlear contents, the later stages of which have been more fully described by Kaida and by Hallpike and Rawdon-Smith. In spite, however, of the difficulties raised by Guttmann and Barrera in their statement of the effect upon the cochlear response of section of the auditory artery, it would seem equally necessary to accept the statement that at any rate in some of the animals the artery was not divided and that in these an uncomplicated degeneration of the cochlear neurones was associated with a normal electrical response.

This finding, in its demonstration of the non-neural origin of the cochlear response, provides a striking contrast to results obtained by Hallpike and Rawdon-Smith in the case of a single animal in which the electrical response was assessed six months after section of the eighth nerve alone. In this animal the response was found to be entirely absent upon the side of nerve section, although the opposite (and unaffected) side showed a response normal in every way, both in the auditory mid-brain, and at the round window. With the exception of gross degeneration of all neural elements, this cochlea presented an appearance altogether indistinguishable from normal. The central canal of the modiolus and the canal of Rosenthal were filled mainly by loose connective tissue and remnants of neurilemmal tissue. Medullated fibres were scarce, and in the space normally occupied by the spiral ganglion only a few atrophied cells could be identified. All the non-neural morphological features, the hair cells, rods of Corti, *stria vascularis* and the inner ear membranes were normal. It may here be pointed out that the attachment of any pathological significance to the slight deviation from normal position of the mem-

brane of Reissner in certain of the cochlear whorls of this preparation was not possible; such deviation as existed was within the limits set by the technical difficulties in preparation of such material, despite the use of gas-free solutions to prevent the development of such pressures as might cause morphological distortion of like character, but greater extent.

The absence of any detectable electrical response in this animal, associated as it was, with complete morphological normality except for the gross neural degeneration already discussed must at first sight be thought to constitute evidence in support of the neural hypothesis of origin of the Wever and Bray effect. It is difficult, however, with due regard to the limitations of histological technique, to attach so great an importance to the results of an operation on one animal alone. Ashcroft, Hallpike and Rawdon-Smith have, therefore, recently undertaken a more complete investigation in which the electrical response from the cochlea was examined in a series of cats, at periods from three days to twenty-one weeks after section of the auditory nerve, and correlated in each case with the histological findings. The results may be described as follows:

In one group of five cases, degeneration of the neural elements and also of Corti's organ was found to have occurred. The electrical responses were however found to be normal or closely approaching thereto.

In a second group of three cases, whereas the neural elements showed advanced degeneration, no significant departure from normality could be observed in the elements of Corti's organ, in particular, in the hair cells. In this group of cases the electrical responses were found to be absent or greatly reduced. The finding in these two groups of cases show that gross degenerative changes in Corti's organ may be associated with a normal electrical response. Conversely, morphological normality of Corti's organ may be associated with absence or gross reduction of the electrical response. The hair cell theory of origin of the Wever and Bray phenomenon would upon this evidence appear untenable. Similarly, the view that the phenomenon originates from action potentials in the terminal fibres of the cochlear nerve would appear equally to be excluded by these findings inasmuch as in all cases degeneration of the nerve elements was found to have occurred. In reviewing the two earlier publications of Guttmann and Barrera, and of Hallpike and Rawdon-Smith in the light of these more recent results, it would appear likely that the cases described by the former may properly be compared to those now

included in Group I, while the single case described by the authors appears to have been reproduced in the cases included in Group II.

(II) *The non-neural hypotheses in the light of the later experimental evidence.* (a) *The Fluid Microphone Suggestion.* This suggestion would appear to be difficult of acceptance in face of the evidence that the electrical phenomena decrease or cease with the injection of cocain via the round window.[3] This method of introduction of cocain to the cochlea through the round window membrane is, however, one in which the possibilities of relatively extensive damage to the delicate cochlear contents cannot be excluded, and for this reason we[18] preferred a method of introduction of cocain wherein crystals of this substance were applied to the round window membrane, the drug gaining entrance to the cochlea by a process of diffusion. It must be admitted that a negative result would have been open to the interpretation that the cocain did not enter the cochlea at all; its entrance is certain, however, in face of the observation that the response did, in fact, suffer a rapid and steady decrease in amplitude, disappearing entirely at the end of an average period of five minutes. This evidence must at first sight be thought strongly to indicate the neural hypothesis of origin of the electrical disturbance; but the evidence that the reduction and abolition of the effect is even more rapid if crystals of sodium chloride are applied to the membrane, in an exactly similar fashion, does not lend material support to this theory.

(b) *The Sensory Cell Hypothesis.* The evidence in favor of this theory of origin of the effect is considerable. The majority of it is summarized by Davis,[8] but a further summary must be given here in order to complete the evidence for and against all the present theories of origin of these phenomena.

It has been reported by several observers[10 20 21] that albino cats, which are congenitally deaf, show no electrical activity from the ear whatsoever. Morphologically, gross abnormalities were found of Corti's organ and its associated membranes. It must be emphasized that although these findings represent a conspicuous advance in localizing the origin of the cochlear response to the scala media and its associated structures, their value in further discriminating between the various hypotheses, neural and non-neural, is limited by the fact that all the structures relevant to these hypotheses, i. e., hair cells, Reissner's and the tectarial membranes, as also the nerve elements, are generally described as being commonly involved in the degenerative process. It should be added that a case has been reported by Lurie, Davis and Derbyshire[25] in which localized degeneration of

the organ of Corti, etc., was demonstrated only in the basal whorl of the cochlea, whilst at the apex a fairly normal histological appearance was found. In this animal a fair response could be obtained from the cochlea for all tones below 250 cycles per second; this response was admittedly somewhat (30 to 40 db.) below normal, but was quite definitely present. Above 250 cycles, the loss of response was progressive, and became absolute for stimuli of frequency above 3,500 cycles. It is thus possible to argue that the presence of Corti's organ is essential for the presence of the electrical cochlear phenomena. More direct evidence in favor of the specific view that it is the sensory cells of this organ which give rise to these effects is contained in the following: by damaging the cochlea in the guinea pig by subjecting the animal for some weeks to a pure tone of frequency 2,500 cycles, and intensity 100 phons, it has been demonstrated[7,8] that the cochlear potentials were much reduced for all stimulating frequencies between 700 and 1,500 cycles. Histological examination showed that, in all the animals, considerable degeneration of the external hair cells had taken place in a wide zone, centering in the middle of the second cochlear whorl. In some animals this area was greater than in others, but in no case had any demonstrable damage taken place to the internal hair cells. Thus a loss of electrical sensitivity, measured in this way, could be correlated with damage to the external hair cells of the organ of Corti. It must however be emphasized that this type of damage is apparently rare, for much greater and nonspecific damage to the inner ear has been reported in animals treated in this way, notably by Wever, Bray and Horton[33] and by Finch and Culler.[11]

Some considerable evidence against the sensory cell hypothesis has recently been published. In the first place, the results of the nerve section experiments already described[4] appear to show, first, that a normal cochlear response may be associated with advanced degeneration of the hair cells of the organ of Corti, and secondly, that a much reduced cochlear response may on occasions be correlated with apparently perfect preservation of these cells.

Further evidence against the sensory cell view is contained in the experiments of Hallpike, Hartridge and Rawdon-Smith.[16,17] They have shown that if the phase of a pure tone stimulus is suddenly changed by 180°, the cochlear response follows this event in such a fashion that its wave form is strictly comparable with that simultaneously recorded with a piezo-microphone. The neural response from the ear, however, exhibits characteristics more in accordance with the view that the vibrating structures responsible for the initiation of the impulses in the acoustic nerve are resonant. From these

results it is, therefore, quite impossible to argue that the structures whose movements are responsible for the cochlear effect are identical with those responsible for stimulation of the eighth nerve. As there can be no reasonable doubt that the hair cells of the organ of Corti are responsible for the latter, they may be excluded as possible originators of the former. These two sets of data appear to argue that the sensory cell hypothesis cannot still be considered as a possible theoretical mechanism.

(c) *The Membrane Hypothesis.* Positive evidence in favor of this theory, which has also permitted its more precise formulation, has recently appeared. It is well known that when a piece of isolated frogskin is so arranged that both sides are bounded by certain fluids, an electrical potential is developed across it.[5 15 29 26] Further, Gatty and Rawdon-Smith[12] have shown that when one side of such a cell is subjected to sinusoidal variations of pressure, for example, to pure tones generated by a loudspeaker and led to the cell by pressure tubing, an approximately sinusoidal e.m.f. closely resembling the cochlear effect in the mammalian ear is produced. Moreover, it has proved possible to indicate the mechanism responsible for this effect in the frogskin. Evidence was produced which pointed to the fact that the amount of internal short-circuiting in the membranes changed as its radius of curvature changed. Thus the alternating e.m.f. produced by the acoustic stimulus was tentatively ascribed to such changes in resistance, and may correctly be considered to be a variation of potential above and below a mean value, according as the pressure gradient across the membrane fluctuates.

Though this evidence is somewhat indirect, it has been urged that this demonstration that movements of a polarized membrane will, in fact, yield an effect similar to that under discussion is in favor of the membrane theory of origin of the latter.

A recent work[4] on the results of section of the eighth nerve in the cat has already been cited as arguing against the sensory cell theory of origin. The authors have, in addition, pointed out that absence of cochlear effect in animals showing a morphologically normal membrane of Reissner may perhaps be ascribed to a failure of polarization of this structure. It was considered possible that such a loss of polarization might be brought about by obstruction to the flow of the perilymph, and further, histological evidence suggesting the presence of such an obstruction of the aqueduct of the cochlea was demonstrated histologically in several of the animals in which the cochlear effect had failed. It was argued that this evidence disposes of Davis' objection to the membrane theory, namely, that in their

earlier work on the results of section of the eighth nerve, Hallpike and Rawdon-Smith had reported an absent electrical response in an animal showing complete morphological normality of this membrane.

It would appear that the balance of the evidence at the moment is in favor of the membrane theory of origin of this phenomenon.

SUMMARY

The first part of this paper concerns the original discovery of the "Wever and Bray Effect." Its discoverers showed that, when electrodes are placed on the eighth nerve of the cat, alternating potentials synchronous with an acoustic stimulus applied to the ear may be readily elicited. Wever and Bray's original view as to the nature and origin of this phenomenon, namely, that the potentials were due to the passage of impulses in the eighth nerve, is no longer held adequate; it is now believed that the effect is of dual origin—in small part due to the passage of impulses, but in greater due to the electrical spread of alternating potentials generated within the cochlea. Section I contains a brief résumé of the various theories which have been propounded as to the origin of this latter component.

This is followed by a fuller discussion of these theories, particularly in the light of the later experimental data. The theories may be conveniently divided into two groups, which have here been termed neural and non-neural. Critical examination leads to the conclusion that, of all of these, the most probable is the so-called "Membrane Hypothesis." On this view the potentials are held to arise owing to movements of a polarized membrane, probably the membrane of Reissner.

REFERENCES.

1. Adrian, E. D.: The Microphonic Action of the Cochlea: an Interpretation of Wever and Bray's Experiments." J. Physiol., 71:28, 1931.

2. Adrian, E. D.: "Discussion on Audition," Physical Soc., p. 5, London, 1931.

3. Adrian, E. D., Bronk, D. W., and Phillips, G.: The Nervous Origin of the Wever and Bray Effect. J. Physiol., 73:2, 1931.

4. Ashcroft, D. W., Hallpike, C. S., and Rawdon-Smith, A. F.: On the Changes in Histological Structure and Electrical Responses of the Cochlea of the Cat Following Section of the Eighth Nerve. Proc. Roy. Soc. B., 122:186, 1937.

5. duBois, Reymond: Untersuchungen über thierische Elektricität. 2:3, 9, 1857.

6. Crowe, S. J.: Anatomic Changes in Labyrinth Secondary to Cerebello-pontine and Brain Stem Tumors. Arch. Surg., 18:982, 1929.

7. Davis, H.: J. Acoust. Soc. Amer., 6:4, 205, 1935.

8. Davis, H., Derbyshire, A. J., Kemp, E. H., Lurie, M. H., and Upton, M.: Functional and Histological Changes in the Cochlea of the Guinea-pig Resulting from Prolonged Stimulation. J. Gen. Phychol., 12:2, 251, 1935.

9. Davis, H., Derbyshire, A. J., and Lurie, M. H.: Modification of Auditory Theory. Arch. Otolaryngol., 20:390, 1934.

10. Davis, H., Derbyshire, A. J., Lurie, M. H., and Saul, L. J.: The Electric Response of the Cochlea. Amer. J. Physiol., 107:311, 1934.

11. Finch, G., and Culler, E.: Effects of Protracted Exposure to Loud Tones. Science, 80:41, 1934.

12. Gatty, O., and Rawdon-Smith, A. F.: Origin of the Cochlear Effect. Nature, 139:670, 1937.

13. Guild, S. R.: Circulation of Endolymph. Amer. J. Anat., 39:57, 1927.

14. Guttman, J., and Barrera, S. E.: Persistence of Cochlear Electrical Disturbance on Auditory Stimulation in the Presence of Cochlear Ganglion Degeneration. Amer. J. Physiol., 109:704, 1934.

15. Hashida, K.: Untersuchungen über das elektromotorische verhalten der Froschhaut. J. Biochem., 1:21, 1922.

16. Hallpike, C. S., Hartridge, H., and Rawdon-Smith, A. F.: Physical Nature of Certain Vibrating Elements of the Internal Ear. Nature, 138:839, 1936.

17. Hallpike, C. S., Hartridge, H., and Rawdon-Smith, A. F.: On the Electrical Responses of the Cochlea and the Auditory Tract of the Cat to a Phase Reversal Produced in a Continuous Musical Tone. Proc. Roy. Soc. B., 122:175, 1937.

18. Guttman, J., and Barrera, S. E.: Persistence of Cochlear Electrical Disturbance on Auditory Stimulation in the Presence of Cochlear Ganglion Degeneration. J. Physiol., 109:4, 704, 1934.

19. Hallpike, C. S., and Rawdon-Smith, A. F.: The Origin of the Wever and Bray Phenomenon. J. Physiol., 83:2, 243, 1934.

20. Howe, H. A.: The Relation of the Organ of Corti to Audio-Electric Phenomena in Deaf Albino Cats. Amer. J. Physiol., 111:187, 1935.

21. Howe, H. A., and Guild, S. R.: The Absence of the Organ of Corti and Its Possible Relation to Electric Auditory Nerve Response. Anat. Rec., 55:20 (Suppl. to No. 4), 1933.

22. Kaida, Y.: Jap. J. Med. Sci., 12:1, 237.

23. Kleyn, A. de, and Gray, A. A.: Notes on a Case of Acusticus Tumour in Which Both Auditory Nerves Were Involved by Separate Growths. J. Laryngol. and Otol., 47:589, 1932.

24. Leiri, F.: Sur la production dans l'oreille interne de phénomènes électriques homorythmiques aux excitants acoustiques. Acta Otolaryngol., 19:265, 1934.

25. Lurie, M. H., Davis, H., and Derbyshire, A. J.: Electrical Activity of Cochlea in Certain Pathologic Conditions. Annals of Otology, Rhinology and Laryngology, 43:321, 1934.

26. Lund, J.: The Electrical Polarity of Obelia and Frog's Skin and Its Reversible Inhibition by Cyanide, Ether and Chloroform. J. Exp. Zool., 44:383, 1926.

27. Rossi, G.: Sulla viscosità della endolinfa e Della Perilinfa. Arch. Fisiol., 12:415, 1914.

28. Siebenman, F.: Diskussion zum Vortrag XV. Verh. dtsch. otol. Ges., 20: 295, 1911.

29. Uhlenbrouck, P.: Über bioelektrische Ströme an der Froschhaut. Zeit. f. Biol., 82:225, 1924.

30. Wever, E. G., and Bray, C. W.: Auditory Nerve Impulses. Science, 71:215, 1930.

31. Wever, E. G., and Bray, C. W.: Action Currents in the Auditory Nerve in Response to Acoustical Stimulation. Proc. Nat. Acad. Sci., Washington, 16:344, 1930.

32. Wever, E. G., and Bray, C. W.: The Nature of Acoustic Response: The Relation Between Sound Frequency and Frequency of Impulses in the Auditory Nerve. J. Exper. Psychol., 13:373, 1930.

33. Wever, E. G., Bray, C. W., and Horton, G. P.: Problem of Stimulation Deafness as Studied by Auditory Nerve Technique. Science, 80:18, 1934.

34. Wittmaack, K.: Über sekundäre Degenerationen im inneren Ohre nach Akustikusstammverletzungen. Verh. dtsch. otol. Ges., 20:289, 1911.

LXXX

BILATERAL XANTHOMATOSIS (LIPOIDOSIS) OF THE MASTOID: CASE REPORT*

V. V. Wood, M.D.

Saint Louis

Xanthomatosis, lipoid granulomatosis or cholesterol granulomatosis, is a disease having apparently to do primarily with a disturbance of the reticulo-endothelial system. The manifestations of the disease have been grouped into several syndromes, some of which are found in the literature, dignified as diseases. To my mind they all are syndromes or symptom-complexes, and the grouping of symptoms depends entirely upon the particular location of the underlying disease.

I found little on the disease in the otolaryngologic literature. The pediatric and radiologic literature was much more fertile. Through the helpful cooperation of Dr. J. A. Rossen we found in the pediatric literature alone at least six classifications of xanthomatosis. These were as follows:

1. Tay-Sachs disease, or amaurotic family idiocy.

2. Niemann-Pick disease, or spleno-hepato-megaly, limited to the Jewish race, and always fatal.

3. Gaucher's disease, or familial splenic anemia, characterized by its frequent familial incidence and by the presence in the spleen of certain large cells with one or more nuclei and a glossy homogenous protoplasm (Gaucher's cells).

4. Schüller-Christian's disease, characterized by decalcification defects in the bony skeleton, exophthalmos and diabetes insipidus.

5. Xanthomatosis. Localized patches of xanthomatosis, variously distributed.

6. Multiple myeloma.

---

*Presented before the combined meeting of the Middle and Mid-Western Sections of the American Laryngological, Rhinological and Otological Society, Chicago, January 11, 1937.

XANTHOMATOSIS

Twenty-five years ago we were taught to recognize yellow raised areas on the eyelids as xanthomatosis of the skin. We were also taught that it was sometimes a sign of diabetes mellitus. I cannot recall anything having been said about diabetes insipidus. During my first few years of medical practice I saw many cases of xanthoma of the eyelids and a great number of cases of diabetes mellitus before seeing the two conditions in combination.

Localized lesions of xanthomatosis in various regions of the body have been reported. In the otolaryngologic literature we find occasionally a case report in which the disease has invaded the field of our specialty. A case of xanthoma tuberosum (raised yellow patches in the soft palate and tonsil) was described by Logan Turner in 1925.

In 1932 Finney reported a case of xanthoma multiplex of the upper part of the repiratory tract in a man aged twenty-seven. He had developed yellowish brown spots, or elevated patches, in the skin, generally distributed over the body. Because of hoarseness and dyspnea the upper respiratory tract was investigated. I gathered from the report that Dr. G. B. New also saw this patient. Lesions were found in the pharynx, hypopharynx, and nasopharynx, with marked scarring. The epiglottis was scarred and covered the glottis so it could not be seen. A tracheotomy became necessary.

In 1936 New reported a case of xanthomatosis of the pharynx, anterior pillars, hypopharynx, epiglottis and vallecula, with pernicious anemia, and another patient complaining of hoarseness, presenting on examination a yellow tumor of the larynx (left side of the pyriform sinus) which was removed by a thyroidotomy with no evidence of recurrence in six months.

In L'Oto-Rhino-Laryngologie Internationale of May, 1937, Pagés reported a case similar to ours and stated that he had found seventy others in the literature. His case came under observation at two and one-half year of age, which he considered the youngest yet reported in the literature. Our patient was only eleven months of age, one and one-half years younger than Dr. Pagés' patient. He considered his case as one of Schüller-Christian's disease, although the exophthalmos was questionable.

SCHÜLLER-CHRISTIAN'S DISEASE

When xanthomatosis attacks the orbits, the hypophysis, the skull and general bony framework, the syndrome known as "Schüller-Christian's" appears. It was first reported by Hand, and is found

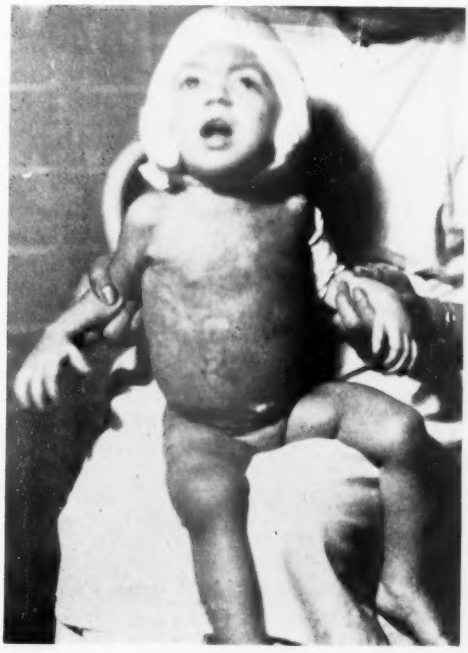


Fig. 1. Showing widely disseminated areas of xanthomatosis of the skin.

listed in the literature as "Hand's disease", "Rowland's disease", and more recently as "Schüller-Christian's disease."

In 1935 Horsfall and Smith, of McGill University, reported a case of Schüller-Christian's disease and, after a meticulous search of the literature, found fifty-nine more, making a total of sixty.

The case we are reporting today does not correspond accurately to the Schüller-Christian's syndrome. Merely a bilateral xanthomatosis of the mastoid with a soft, flabby tumor over the left triceps was present when the patient was first observed. No exophthalmos and no diabetes insipidus was present, and no other bony defects appeared on the x-ray films of the entire bony skeleton. Repeated x-ray studies failed to reveal any new areas of bone disease until the last series of films was taken on January 2, 1937. These showed several new areas of decalcification in the skull, two small areas in

the left tibia and defects in each seventh rib. All these new lesions had developed since the last series of plates was taken on October 6, 1936. At no time did any diabetes insipidus or exophthalmos appear. Dr. Rossen thought it to be a case of potential Schüller-Christian's disease and Roberts of St. Louis University suggested that in time the entire syndrome would probably develop. The slides of the mastoid lesions were shown to several pathologists in St. Louis. All agreed on xanthomatosis and probably a beginning Schüller-Christian's syndrome, except one. This pathologist at first agreed with the others, but he was probably influenced by my description of the clinical and the macroscopic pictures. Eventually, however, he decided that it might be a mistake to report this case as xanthomatosis because microscopically it appeared to be a lymphosarcoma. To my mind the mastoid lesions could be classified accurately as xanthomatosis of the skull, both clinically and macroscopically. I therefore sent a slide to Lee M. Hurd of New York with the request that he get an opinion from James Ewing, if possible. An abstract of Ewing's prompt reply to me follows:

"In this laboratory we think the tissue shows a pronounced case of Christian-Schüller's disease, which is essentially xanthomatosis. The tissue is remarkably cellular and looks almost like lymphosarcoma. That it is not lymphosarcoma is shown by the pale staining of the cells, by typical fat giant cells, and by characteristic xanthoma cells on the outskirts of the lesion. I presume that true liposarcoma sometimes results on the basis of this process, but I do not think your case is malignant."

The patient entered St. Mary's Hospital during my absence from St. Louis. Therefore I did not see her on admittance. The first operation on the right mastoid was performed on June sixteenth by one of my associates.

The history obtained at the time of admission to the hospital was more or less unreliable due to the fact that relatives brought the child and knew little about the exact facts. However, it was roughly gathered that swellings were noted behind the ears some time in March, 1936, first on the left, and then on the right side. Later, during the month of May, 1936, the ears began to discharge, at first the right, and then the left ear. The postauricular swelling persisted. No history of earache or fever was obtained. Therefore nothing could be found in the history to suggest an inflammatory onset.

The child was a full term baby and was delivered spontaneously. She was breast fed and had had cod liver oil and orange juice. She

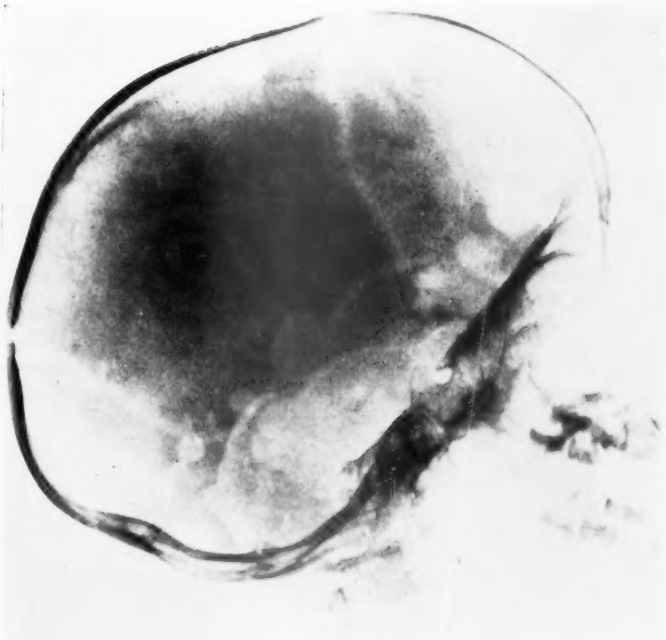


Fig. 2. Showing numerous decalcified areas scattered throughout the skull.

had always been a poor eater. There was no significant family history. There were two siblings, both living and well.

This was a well-nourished, well-developed female child, eleven months of age, not acutely ill. There were fluctuant and tender swellings behind both ears, both auricles protruded. The left canal wall was swollen; the ear drum could not be seen. The right canal was full of pus. The child had three upper and two lower incisor teeth. There was a macular rash on left arm, chest, and labia majora.

The first operation was performed by Dr. M. A. Webb on June 16, 1936, and his own description of the operation is given. "The usual postauricular incision was made. The entire right mastoid cavity was filled with what appeared to be fatty tissue with complete destruction of entire bony cortex in the middle and posterior fossæ. The destruction of bone extends to the labyrinth or at least one-

eighth inch below the antrum. The antrum was filled with the same tissue. No pus was found. The mass was removed with the gloved finger. The antrum was identified and in attempting to curette tissue out of this area the incus and malleus were removed. The mastoid cavity was packed with iodoform gauze and closed with clips."

There was considerable postoperative shock; the patient almost expired on the operating table. Oxygen was administered and fluids were given subcutaneously. The patient was in much better condition by the next day. Her temperature varied from 102 to 106 degrees and she was very pale, but took her feedings well.

Sections of the tissue removed at this operation were examined by Dr. Roberts, who made the following statement: "Sections . . . . show a granulomatous reaction. The tissues are composed of reticuloendothelial cells (or macrophages laden with lipoid material). Large giant cells are numerous . . . . also many polymorphonuclear cells (neutrophils, eosinophils and a few embryonic blood cells). No organisms of the infectious granulomatous diseases can be found. The clinical history, plus the bone involvement and the sections all taken together, speak for a lipogranulomatosis (xanthomatosis) or metabolic fat disorder, apparently Schüller-Christian disease."

The second operation was performed by the author on June 18, 1936. Curvilinear incision behind left ear uncovered a large conglomerate mass of soft fatty tissue entirely surrounding the attachment of the pinna from the mastoid tip upward above and down in front of the tragus to about one inch below the level of the zygoma. When this tissue was removed to the level of the mastoid cortex it was found that the entire mastoid was destroyed, decalcified and replaced by the growth. Both inner and outer tables were gone. No dura could be identified. The growth had apparently invaded the dura and the brain, as it had the mastoid cells, subcutaneous tissue and skin. The finger could be inserted for an inch or more below the level of the inner table into a yielding soft mass having no more resistance than softened brain. The root of the zygoma was gone and there was no bony floor to the brain from that area backward to the posterior border of the mastoid. The fatty greasy mass was spotted with areas of deeper yellow and was very vascular—many large and small blood vessels ramifying everywhere.

The character of this pathologic process being so uncertain and its invasion of surrounding structures so uncircumscribed no attempt was made to clean out all diseased tissue. This was obviously impossible. The wound was packed with iodoform gauze and partially closed, but left open for one and one-half inches at the lower angle.

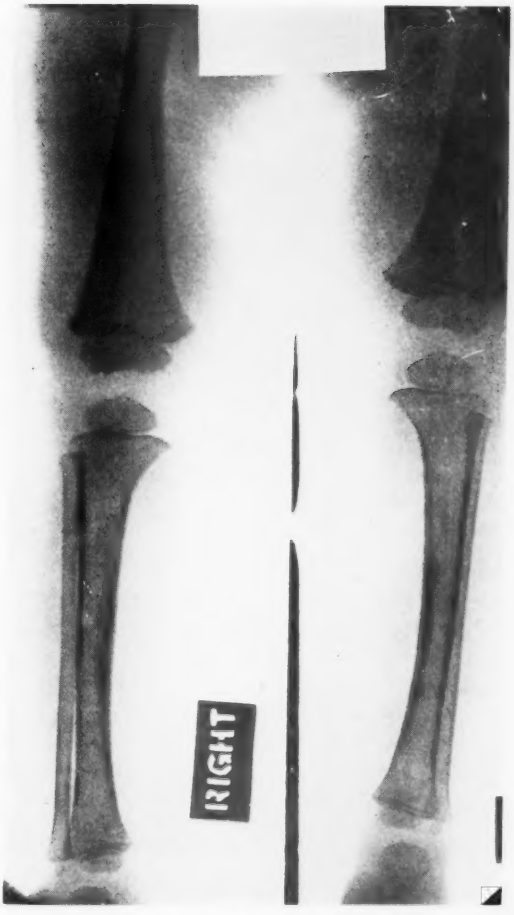


Fig. 3. Showing two small decalcified areas near the middle of the right tibia.

The patient was in the hospital from June 16, 1936, until her death, January 12, 1937. A detailed account of her progress, laboratory studies, and treatment would be lengthy, therefore a brief synopsis of the records will be recorded.

She declined progressively until death occurred of a terminal pneumonia January 12, 1937.

X-ray studies of the entire bony skeleton were carried out by Dr. L. R. Sante at suitable intervals. Films were made on the following dates: June 23, July 30, September 9, October 6, and January 2. As previously stated, no progress of the disease was noticeable until the last series was taken January 2, 1937. This showed a decided spread of the disease throughout the bony skeleton since the previous October. The mastoid lesions were larger, and many new areas of decalcification appeared in the skull, distributed widely throughout the calvarium. Both seventh ribs had been attacked and a large portion of the right in its lateral and anterior aspect was missing. A smaller area of the left rib near the mid-axillary line was decalcified. Two small areas of decalcification appeared in the right tibia.

The mastoid wounds never healed completely. Considerable effort at repair seemed to manifest itself, but an area of exuberant raw unhealed tissue was always present. Clinically the raw areas were chiefly composed of granulation tissue.

The subcutaneous nodules constantly increased in number and in width of distribution. Erythematous skin lesions began to appear on the trunk early in September, together with scattered petechiae. These lesions gradually became raised and papular and increased in size and distribution. Biopsy demonstrated them to be areas of xanthomatosis of the skin. Edema of the feet was noted on September 26, 1936. A troublesome seborrhea of the scalp appeared during the last week of July and persisted in spite of treatment. On November 8, 1936, gingivitis developed, the gums were sore and swollen.

No exophthalmos or diabetes insipidus ever appeared.

A low irregular fever alternated with periods of higher constant temperature which we could not adequately explain. The chart suggested central pneumonia during some periods but it could never be found by stethoscope or x-ray.

The patient became progressively more emaciated and dehydrated. Her weight steadily fell although some gains occasionally occurred. The mental attitude was always abnormal and morose; she was never cheerful and there was no tendency to play; sometimes

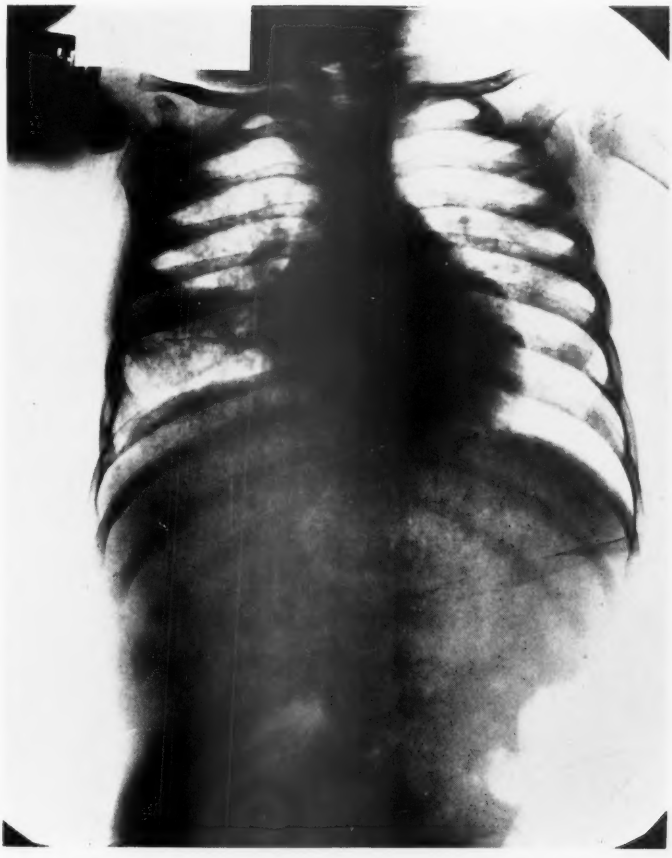


Fig. 4. Showing the large defect in the right seventh rib and a small decalcified area in the left seventh rib.

listless, she often slept for long intervals, but when awake she seemed to be unhappy or suffering.

LABORATORY EXAMINATIONS

Blood Counts: June 16, 1936 (day of admission to hospital); red blood cell count, 3,800,000; hemoglobin, 70 per cent; white blood cell count, 23,400; differential count—juveniles, 2 per cent; stab cells, 15 per cent; segmented neutrophils, 31 per cent; lymphocytes, 50 per cent; monocytes, 2 per cent.

July 4, 1936—Red blood cell count, 3,200,000; white blood cell count, 15,000; reticulocyte count, 1.1 per cent; platelet count, 150,000.

September 4, 1936—Red blood cell count, 4,240,000; platelet count, 144,000.

October 13, 1936—White blood cell count, 4,680; differential count—juveniles, 2 per cent; stab cells, 12 per cent; segmented neutrophils, 21 per cent; basophils, 1 per cent, lymphocytes, 57 per cent; monocytes, 7 per cent; hemoglobin, 95 per cent.

November 4, 1936—Red blood cell count, 2,960,000; white blood cell count, 6,000.

Bleeding and Clotting Time of the Blood—September 4, 1936—Clotting time, 1½ minutes; bleeding time, 4 minutes.

October 13, 1936—Clotting time, 1 minute and 20 seconds; bleeding time, 3 minutes and 10 seconds.

October 20, 1936—Clotting time, 6 to 7 minutes (multiple tube method).

Capillary Resistance Test—October 7, 1936—Capillary resistance is abnormally low, petechiae form in less than 30 seconds on the arm, if the return flow of venous blood is constricted.

Blood Chemistry—July 4, 1936—Plasma cholesterol, 246 mgm. (normal is 140 to 170 mgm.);

August 19, 1936—Sugar, 75 mgm.; non-protein nitrogen, 33 mgm.; calcium, 9.1 mgm.; chlorides, 544 mgm. (normal is 480 to 520 mgm.).

October 15, 1936—plasma cholesterol, 192 mgm. (normal is 140 to 170 mgm.); sugar, 87 mgm.; non-protein nitrogen, 33 mgm.; chlorides, 593 mgm. (normal is 480 to 520 mgm.).

Bacteriology—September 4, 1936—Blood culture, sterile.

October 1, 1936—Culture of stool for typhoid and dysentery bacilli, negative; test for occult blood in the stool, negative.

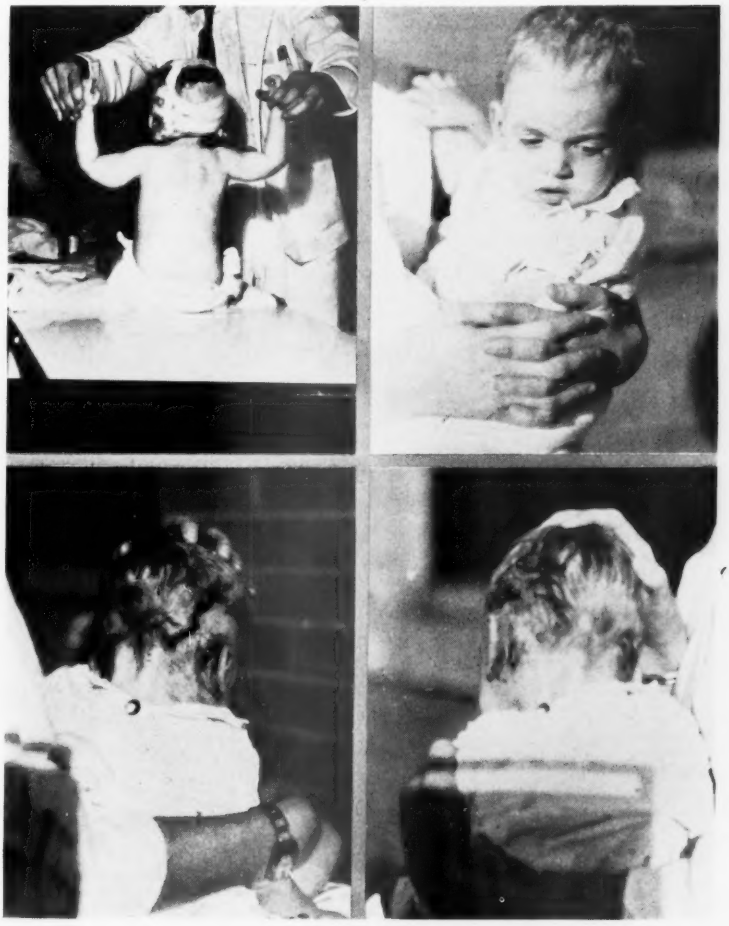
October 20, 1936—Blood culture, sterile.

Schick Test—August 5, 1936—Negative.

Tuberculin Test—August 5, 1936—Negative.

SUMMARY OF TREATMENT

1. *Local Treatment of Wounds*: Skin clips were removed from both mastoids on June 24, 1936, and gauze packs were removed from the right side. A small rubber tissue drain was reinserted. Daily dressings of the wounds were begun June 29, 1936, when gauze packs



5A 5B
5C 5D

Fig. 5A. Showing the subcutaneous nodule over the left triceps.
Fig. 5B. Showing absence of exophthalmos in a full-face view.
Fig. 5C. Showing right mastoid wound—absence of complete healing.
Fig. 5D. Showing left mastoid wound—absence of complete healing.

were removed from left side and all drains removed from right. Following these early dressings the wounds were given x-ray treatments. Silver nitrate, forty per cent solution, was used to keep down exuberant granulations and dressings were changed as frequently as necessary for surgical cleanliness. Dakin's solution was used occasionally. Crusts were removed with peroxide. Protective salves and staphylococcus antiseptics were occasionally used. No impetigo or spreading secondary infections occurred but, as previously stated, complete healing was never obtained.

2. *X-Ray Treatment*: The x-ray treatment is described by Dr. Sante in the following protocol: "Recorded cases of Schüller-Christian's disease show response to x-ray therapy with filling in of the bony defects after five to six months. Treatment of this sort, varied in the literature from 140 kilovolts with 3 millimeters of aluminum filter to 200 kilovolts with 1 millimeter copper and 1 millimeter aluminum filter. The quantity of radiation delivered varied from 33 per cent of an erythema skin dose to almost 100 per cent. In later years dosage has been expressed in R units— as much as 600 R measured in air has been used. Good results have been obtained no matter what voltage was used as long as sufficient dosage was given. Since treatment is directed to areas of bone destruction only it was thought advisable to utilize superficial radiation therapy. To this end the following course of x-ray therapy was administered:

July 30, 1936—95 KV. (6-in. spark gap), 4 Ma., 40 cm. distance, 4 min. time. 160r given over defects in skull.

August 1, 1936—Similar factors used; 4 min. 160r given over defects in skull.

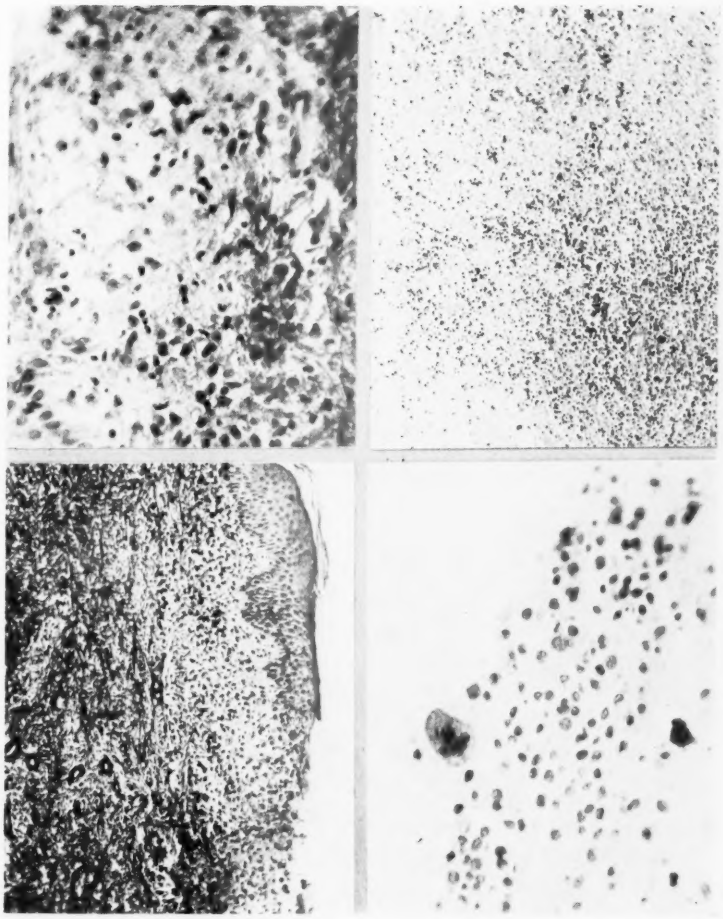
August 5, 1936—Similar factors used; 3 min. 120r.

The areas were observed for a period of 5 months. At first there seemed to be little change, but within the last few months there has been not only distinct enlargement of the areas already existing near the mastoid areas, but new areas have appeared elsewhere in the skull and in other bones of the body.

Further radiation therapy has been outlined using higher voltage as follows:

January 7, 1937—135 KV. (9-in. spark gap) 5 Ma., 40 cm. distance, 10 min. time, 220r (measured in air) given over both sides of entire skull.

January 8, 1937—Similar factors used for treatment of defects in 10th rib on both sides, and in long bones.



6A 6B
6C 6D

Fig. 6A. Microphotograph of tissue from mastoid, high power showing foam cells and giant cells.

Fig. 6B. Microphotograph of tissue from mass over left triceps, low power.

Fig. 6C. Showing Microphotograph of skin lesion. The eroded area at upper right corner of photograph shows destruction through epidermis by lesion of xanthomatosis.

Fig. 6D. Microphotograph showing a large giant cell.

3. *Heliotherapy:* Sunlight and ultraviolet light were also used. Daily exposure to sunlight began September 9, 1936, and continued until October 21, 1936, when daily exposure to ultraviolet lamp was substituted.

4. *Vitamin Therapy:* Vitamins A and D in the form of cod liver oil, one drachm twice a day, and later viosterol.. Vitamin C (Cebione 0.05 gram intramuscularly), orange juice. McKinney's Vitamin B Extract 15 minims twice a day.

5. *Organotherapy:* Thyroid extract begun daily July 3, 1936. Insulin: 2 units twice a day begun September 9, 1936, and discontinued October 2, 1936, when Liver extract (Lederle) 1 cc. intramuscularly every three or four days was begun. Pituitrin was also used.

6. *Foreign Protein Therapy:* Blood transfusions and whole blood intramuscularly.

7. *Diet:* General.

8. *Miscellaneous Medication:* Dicalcium phosphate begun September 5, 1936. Stimulants. Cathartics, p.r.n. Sodium perborate mouth wash for gingivitis begun November 8, 1936.

The autopsy was unsatisfactory and disappointing because the family stubbornly refused to permit an examination of the brain which was the area in which I was chiefly interested. We had nearly everything else; however, the findings in the internal organs were interesting. What I wished to learn most of all was whether or not the disease had actually invaded and destroyed the dura and entered the brain substance as a malignancy might have done. I had visualized such an invasion founded upon my impressions at operation.

A protocol of the autopsy findings by Dr. Roberts is appended.

PATHOLOGIST'S REPORT

Surgical Pathology: Material received from both mastoids consisted of numerous small bits of friable tissue. They were irregular in shape and none measured over one centimeter in the longest plane while most of them were not over a few millimeters. For the most part they were yellowish-white in color, although a few were red with hemorrhage. All were soft in consistency resembling brain or a very cellular sarcoma. They had been fixed in formalin when submitted to the pathologist. The microscopic examination of these pieces revealed lesions which were at first thought to be granulomatous in nature. While there was considerable variation in cell types the

predominating cell in all was a large, pale cell which was round or oval in shape. Its nucleus stained well and was either centrally or peripherally placed. Nucleoli were frequent. The cystoplasm was distinctly vacuolated in most cases. It was considered to be monocytic. Giant cells were abundant in many fields. They were of foreign-body type and had foamy or vacuolated cytoplasm. The other cells, which were anything but constant in number, were neutrophils, eosinophils, lymphocytes and plasma cells. Capillaries were not very common. In places fibrosis could be made out. While some of the areas were circumscribed they did not closely simulate tubercles of the infectious granuloma. Repeated mitotic counts revealed less than one mitosis per 1000 cells. The diagnosis reported was that of lipoidosis, probably Schüller-Christian syndrome.

Surgical Pathology: The gross material received, having been removed from the left arm, was a small yellowish-white mass. It was quite plastic and appeared to be very necrotic.

The microscopic findings in this tissue were about the same as those found in the biopsy taken from the mastoid region. There had been considerable necrosis but a few islands of well preserved tissue remained. The cells were chiefly monocytes, the cytoplasm of which contained a great amount of fatty material. The cellular infiltration, because of the necrosis, contained a higher percentage of neutrophils. Giant cells were of enormous size in this lesion and were vacuolated. A Nile-blue sulphate stain was done on this tissue and the result was positive for cholesterol compounds. The mitotic count was below one per 1000 cells. The diagnosis was reported as unchanged.

Autopsy: For the sake of brevity, weights and measures on the body and organs have been eliminated so that this report includes only positive findings or relevant information.

External Examination: The body development had been good but the state of nutrition was poor. The skin revealed an exceedingly great number of lesions. These were most abundant over the trunk but were numerous over the thighs, neck, cheeks, nose, scalp and extremities. They were bright red and appeared as puncta or macules. The skin felt thickened about these lesions. The hair of the scalp was of fine texture and was matted together with a greasy material which was soluble in fat solvents. There was an undue prominence of the left parietal boss. Just behind this was a noticeable flattening of the bone. In the glabellar region was a deficiency in the frontal bone. This was irregular in shape but was approximately fifteen mm. in

diameter. The mastoid wounds contained a greasy necrotic material which was grayish-yellow in places and purplish in others. The mouth showed malocclusion of poorly formed teeth. The gums, at their free margins, were soft with necrosis and were quite dirty. There was a healed incision of the medial surface of the left arm. On the antero-lateral aspect of the right thigh was a small, soft tumefaction which was attached to the skin. It contained a yellowish-gray semi-fluid material.

Internal Examination: There was a fusiform swelling of the right and left seventh ribs which bulged into the pleural cavities. The swellings were soft and hemorrhagic. The right revealed a pathological fracture. Other than the above changes, the pleural, peritoneal, and pericardial cavities were essentially normal.

Heart: The heart revealed no gross change in size, consistency, in measured thickness, or in weight.

Aorta: The aorta appeared normal in diameter, thickness, elasticity and in smoothness.

Lungs: The lungs completely filled the pleural cavities. They were mottled yellow and purple. Their density was increased while their crepitance was decreased throughout. Numerous tiny emphysematous patches were present.

Liver: The liver was smooth and tense. Its substance was somewhat friable and was mottled brown with yellow. There was some question as to possible yellow dots on the cut surface.

Gall-Bladder: The gall-bladder was grossly normal and the biliary duct system was patent.

Pancreas: Nothing of interest could be found in the examination of the pancreas.

Stomach and Intestines: Except for autolytic changes of mucosa of the gastro-intestinal tract these parts were not striking.

Spleen: The gross spleen appeared to be about twice the normal size. There was also a tiny accessory spleen present. The cut surface of the spleen was of deep purplish color while its consistency was soft. At its inferior border was a white, firm area about fifteen by five mm. which had the appearance of an anemic infarct.

Suprarenal Glands: Nothing of gross interest could be seen in the adrenal glands.

Urinary-Bladder: The urinary-bladder presented nothing in the way of gross morbid anatomy.

Kidneys: The kidneys were of about normal size, weight, and shape. Markings were distinct and the proportions of cortices to medullae were as usual. Capsules were not adherent. No infiltrations could be seen. The pelves and ureters were not interesting.

Adnexa: The uterus, tubes, and ovaries were normal for the age.

Thymus: The thymus was not remarkable in size or in substance.

Thyroid: The thyroid was grossly unchanged.

Lymph Glands: The lymph glands of the mesenteries and those about the abdominal aorta were enlarged and even more so than would be expected for the age. They were soft and pinkish-gray in color. The solitary follicles of the colon were prominent.

Brain: No permission for the examination of the central nervous system could be obtained.

Microscopic Notes: Sections made of lungs, kidneys, liver, skin, ribs, gums, tumor of thigh, mastoid wounds and lymph glands (mesenteric, gastro-hepatic ligament and near cardia of stomach) all show the lesion described as Schüller-Christian disease. Less characteristic, but probably belonging to this disease, were lesions in the spleen, accessory spleen, colon, and pancreas. No lesions of the disease could be seen in the aorta, thymus, heart, thyroid, adrenals, and muscle.

In many cases the lesions were fairly dicrete nodules. However, in many other instances, the usual cellular reactions were seen but they did not have the granulomatous appearance but were more diffuse as if infiltrations. The constant finding was that of large, pale cells with small nuclei and with cytoplasms which were vacuolated or foamy. The paraffin sections gave the appearance of having had something dissolved out of their cytoplasm. They were monocytic or reticulo-endothelial. Giant cells were abundant and had the cytoplasmic changes seen in the case of the monocytes. In practically all lesions were found rather abundantly eosinophils and neutrophils. In a great many cases lymphocytes and plasma cells were seen. The cellular variation was probably due to the age of the lesions. In a few lesions, such as one rib, considerable fibrosis had occurred as if the lesion were old. The mitotic figures were too scarce, in all cases, for

one to admit a malignant tumor. In many cases, as pointed out by Rowland, definite perivascular reactions could be seen.

Other than the Schüller-Christian disease very few pathological changes could be found. There were advanced changes in parenchymatous tissues of heart, kidney, pancreas, and muscle but these could be either cloudy swelling or postmortem autolytic changes.

BEAUMONT BUILDING.

LXXXI

PROGRESS IN LARYNGOLOGY*

LEROY A. SCHALL, M.D.

AND

JOHN R. RICHARDSON, M.D.

BOSTON

The sympathetic innervation of the nose has been the subject of investigations by Larsell and Fenton,[1] Higbee,[2] Kuntz[3, 4] and St. Ernyei.[5]

Larsell and Fenton[1] take up in detail the pathways of referred pain and the reflex arcs involved. The several possible vasoconstrictor and dilator reflex arcs that are pathways for impulses clearly explain reflex vasomotor disturbances.

The fundamental division of the nervous system is, of course, into the sensorimotor and autonomic systems, and as Higbee[2] emphasizes, the autonomic system is the efferent system, distributed to glands, smooth muscle and blood vessels, and concerned only with vegetative functions.

Kuntz[3] brings out the relation to allergy. He states:

> The autonomic innervation of the mucous membranes and involuntary musculature of the upper respiratory tract, the paranasal sinuses, the middle ear and the auditory tube includes both sympathetic and parasympathetic nerves. The functional state of the mucous membranes, including their secretory and ciliary activity, is regulated and controlled through the autonomic nerves and is intimately related to the functional state of the peripheral blood vessels. Inflammatory reaction differs only in degree from the normal physiological response.
>
> That the autonomic nerves are at fault in allergic disorders is indicated by the sudden appearance of their manifestations. In cases of allergic rhinitis the water content of the nasal secretion is increased and the calcium content diminished. The reduction in the calcium content of the nasal secretion is probably an expression of a shift in the acid-base balance of the body fluids toward alkalinity. The acid-base balance, which is closely associated with the autonomic balance, must therefore be regarded as an important factor in the etiology of allergy.
>
> Therapeutic measures designed to restore the acid-base balance, and consequently the autonomic balance, seem to be indicated in allergic cases and in various other conditions in which the functional activity of the respiratory mucous membranes is disturbed.

*Printed in full with the permission of the New England Journal of Medicine.

Vessels of the cavernous or erectile tissue in the nasal mucosa react to nerve stimulation in a manner differing from that of the vessels in the adjacent mucous membrane.

In regard to pathways of referred pain, Kuntz[4] states:

Certain pains in the neck, upper thorax and upper extremity which are associated with lesions in the mucous membranes of the nose and paranasal sinuses exhibit the characteristic features of referred pains. In view of the anatomic data which indicate that efferent components of the upper thoracic spinal nerves traverse the plexuses on the common and internal carotid arteries and reach the mucous membranes of the nose and paranasal sinuses, these pains may be regarded as referred, in conformity with Head's theory of the localization of referred pains.

Referred pains are accompanied by reflex phenomena which play a part in the causation of the sensations of pain. Impulses directly responsible for sensations of pain probably arise in pain receptors in the peripheral area in which the pain is localized. The stimulation of these receptors is caused by the reflex responses, probably through the accumulation of waste metabolites or the liberation of a stimulating chemical substance.

The mechanisms involved in the components of the referred pains in question which are due to reflex phenomena may be outlined as follows. Impulses arising at the site of a lesion in the nasal or paranasal mucosa are conducted into the spinal cord through afferent components of the upper thoracic nerves, reach the corresponding ganglia of the sympathetic trunks through preganglionic neurons, and are conducted to the periphery through sympathetic neurons. Pain receptors at the periphery are stimulated; the impulses arising in them are conducted into the spinal cord through afferent components of the corresponding spinal nerves and upward through the lateral spinothalamic tract on the contralateral side.

St. Ernyei[5] carried out histologic studies on white rats, guinea pigs and cats. He investigated the finer distribution and connections in the nasal mucous membrane of the olfactory, trigeminal, sympathetic and nervous terminals.

Lyman[6] has summarized the work of Sluder on the sphenopalatine ganglion. Sluder published thirty-five papers devoted to the syndrome of this ganglion.

In the diagnosis and treatment of neuralgia, Hoover and Poppen[7] state:

Trigeminal and glossopharyngeal neuralgias are alike in all respects except the location of the agonizing flashes of pain and the location of the "trigger" areas. The areas in glossopharyngeal neuralgia include the pharyngeal wall, tonsillar area, the base of the tongue and occasionally the ear, while in trigeminal neuralgia they are the mucous membrane about the mouth, lips, nose and various areas on the face. In all cases careful examination should be made of the larynx, upper end of the esophagus, the palate, tonsils and posterior molar teeth, because malignant conditions in these regions may produce symptoms suggestive of a glossopharyngeal neuralgia.

Alcoholic injection is not feasible because of the smallness of the nerve and its very close relation to the vagus, jugular and hypoglossal nerves. Inhalations of

from fifteen to thirty drops of trichlorethylene three or four times a day have really been very efficient in giving marked relief from this condition. The surgical treatment of choice is the intracranial section of the ninth nerve in the posterior fossa. This exposure makes it possible to exclude tumors in this area. Following intracranial section of one glossopharyngeal nerve, patients are not conscious of any paresthesia or discomfort whatsoever.

EXTERNAL NOSE

An instance of primary hemangioma of the nasal bone is described by Neivert and Bilchick.[8] This seems to be the first case of this condition reported.

Biegeleisen[9] presents a new treatment for the embarrassing telangiectases of the nose. Until now there has been no satisfactory treatment. The author describes a micro-injection technique based upon the treatment of similar lesions on the legs. A special needle is employed to inject 30 per cent sodium chloride directly into the capillary lumen. The author states that the method is safe and cosmetically good.

Benjamins[10] describes several cases of congenital epidermal fistulas and cysts of the nasal bridge. These are illustrated by photographs and by radiograms showing the passages and cysts after injection with lipiodol. The only effective treatment, he says, is complete removal by dissection of the entire fistulous tract and cyst, and this is rendered much less difficult if the lumen is stained by the previous injection of methylene blue.

Weinhold[11] presents two cases of infection of the nasal vestibule from vaccine pustules in which the diagnosis was specially difficult and could be made only after a careful consideration of the clinical history. The patients were women; the condition developed rapidly, resembling herpes, acute eczema, or perhaps the more chronic forms of erysipelas. There was some ulceration in the nasal vestibule, crusting, and considerable swelling of the nose and upper lip. The acute inflammation and all the symptoms subsided after about ten days. Both the author's patients were in contact with infants who had been successfully vaccinated some twenty days beforehand.

NASAL AIRWAYS

Buhrmester[12] has continued her studies on the chemical composition of nasal mucin. She finds it to be unlike mucin from other tissues.

Buhrmester and Wenner[13] show that nasal polyps and normal mucous membrane contain a histamine-like substance in approximately equal amounts in the moist tissue. Calculated on the basis of

the dry weight of the tissue, polypoid tissue contains more histamine than the normal membrane. Nasal secretion from persons with allergic rhinitis does not have depressor activity when injected intravenously. The hydrolyzed secretion contains much less histamine-like substance than do polyps, calculated on equal protein values. Histaminase is not present in allergic nasal secretions. These writers suggest that the increase in mineral content of the nasal discharge, with its resulting effect on permeability, difference in potential and acid-base equilibrium, is a factor to be considered in studying the formation of polyps and other allergic manifestations.

Chavanne[14] in a long series of experiments on dogs demonstrates energetic limitation of nasal secretion when thyroxin is injected intravenously. Thyroidectomy seemed to increase the amount of nasal secretion, which could readily be reduced by systematic injection of thyroxin.

Zaritzky[15] describes the changes in the mucous glands and cavernous tissue of the nose due to age.

Certain methods of demonstrating organisms in the nasal mucous membranes, such as microscopic examination of smears from swabbings, tissue sections or cultures, and animal inoculations, have been used by the majority of investigators in the field of nasal bacteriology; however, so far as the literature suggests, the use of epithelial scrapings in demonstrating organisms in the nasal mucosa has been employed infrequently, if at all. Schuster[16] states:

> This method of epithelial scraping offers certain advantages in the study of nasal bacteriology in general, and is of particular value in showing the existence and incidence of tubercle bacilli in the mucosa of the tuberculous.
>
> Of the 50 unselected cases of pulmonary tuberculosis, 30 per cent showed tubercle bacilli in the epithelial scrapings, but in the nasal smear of these same cases no organisms were found. Entrance of tubercle bacilli into the nasal mucous membrane may be an ectogenous invasion caused by fingers, handkerchief or bacilliferous sputum, or endogenous by way of the blood stream and lymphatics.
>
> Patients showing positive tubercle bacilli in the nasal mucosa may possibly be considered as potential cases of nasal tuberculosis.
>
> Since 28 per cent of the positive cases yielded variation or granular forms of the organisms but only 16 per cent yielded rod forms, and since the variation forms are avirulent or dead organisms, and since the latter forms are found where the lytic action or the resistance toward the organism is great, one may possibly conclude that many cases of primary nasal tuberculosis are caused by avirulent or dead tubercle bacilli or their chemical products.
>
> This method of epithelial scraping may be of value in studying the nasal bacteriology in different acute and chronic infections of the mucosa. Since the bacterial flora of the nose is so complex, and since it is difficult to determine which

organism is the true infective agent, it is correct to conclude that the organism or organisms found subepithelially are probably the predominating organisms in the disease, and more than likely are the causative factors.

Snyder and Feldman[17] record three cases of rhinoliths. All are of the false variety. The first was due to a sponge retained in the nose following an operative procedure. The second showed a shoe button to be the obstructing factor. In the third the nucleus was a piece of twine; in this case the patient, so far as we can ascertain, was the youngest on record with a rhinolith, being only six years old.

Goodman[18] writes on nasopalatine duct cysts. These form in the incisor canal region of the maxilla from epithelial cell rests of a persistent nasopalatine duct. They have no direct relation to the teeth, but in their growth may encroach upon the incisor apices. Such cysts produce an expansion of the bony canal, lined with epithelium and containing fluid. The onset may be insidious, without symptoms, the cysts being discovered on routine x-ray examination of the teeth. Larger nasopalatine duct cysts may give rise to definite pains, which are usually of a neuralgic character and may radiate to the nose or the eyes or along the roof of the mouth. Swelling of the papilla palatina may occur. Tenderness is often elicited on pressure or percussion over the anterior incisor region.

Goodman states that surgical removal and curetting of the areas of the cyst are indicated when repeated swellings of the papilla palatina have occurred or where there is a history of neuralgic pains radiating along the roof of the mouth or the nose or to the orbital region. Removal of the upper incisor teeth in the involved area is rarely if ever necessary since nasopalatine duct cysts are not of dental origin. When, upon expansion, the cyst affects the roots of the adjacent incisor teeth and causes erosion, apicoectomy can be done. In the absence of symptoms or of an increase in size of the area of decalcification caused by the cyst, surgery is not indicated.

The usual site of mixed tumors is the parotid region. These tumors rarely appear in the upper air passages and accessory sinuses. They seem to be most uncommon in the nasal septum. In 1932 Stevenson reported a case of mixed tumor of the nasal septum. He stated that careful search of the literature had failed to reveal mention of such a tumor before his own report. Weidlein[19] has not found any case reported since Stevenson. He gives one case in detail. He[20] also lists three cases of hemangioma of the septum cured by excision.

Richter[21] advances evidence to the effect that congenital bending of the nasal septum is frequently a result of the primary enlargement of one or several of the nasal conchae. He points out that such hyper-

plasias occur during the embryonal period, he himself having made observations on human embryos which indicate this. He thinks that such hyperplasia may be of inflammatory or other origin.

Laszlo[22] gives many practical points regarding submucous septum resection. He agrees that the rigid rule that no operation on the septum should be done until the nose is fully developed, usually at the age of eighteen, cannot be strictly adhered to. There are many cases that require an operative procedure as early as eight to nine years of age. In cases where the deviation is very marked and the nasal difficulties are severe, careful removal of the deviated cartilage or bone will be a great advantage to the general development of the child and in turn will help to ameliorate the local symptoms. Removal of parts should be limited to those necessary to establish adequate nasal breathing. Radicalism, which is very important in adults, should be excluded when one is operating on a developing part of the body.

Ombrédanne and Causse[23] operate even earlier. They contend that the customary diffidence in operating on the deviated septums of children is exaggerated. They supported this contention by bringing before a meeting two cases in which they had operated with extremely good results; the ages of the patients were one year and six and a half years. The authors believe that it is bad surgical practice to leave a septal deformity uncorrected when the deformity is obviously interfering with the child's development.

Sternstein[24] studied 32 adults in a series of 140 experiments to determine how much resistance air encounters in its passage through the nasal airways independently of voluntary nasal breathing. A special apparatus and simple technique were employed. The resistance measurements clearly presented a visual record of the amount of obstruction encountered in the nasal chamber.

Moncrieff[25] says that in nasal obstruction of the newborn the urge to breathe through the nose is so strong that not infrequently, when nasal obstruction is present, the baby will die rather than develop mouth breathing in the early days of life. Mouth breathing is not acquired until the age of from ten to fourteen days. Thus in all instances where there is difficulty in breathing in the newborn baby the state of the nasal airways should be carefully examined, and any narrowing be dealt with, if possible, by the passage of a soft rubber catheter.

Van Gilse[26] and Kearney[27] present cases of complete bony atresia of the posterior nares.

Nasal hemorrhage, usually easy to stop, sometimes requires heroic measures. Goodyear[28] gives the etiology and accepted forms of treatment from the simplest to the most radical needed to control hemorrhage of the nose and throat. He[29] reports a case with intractable bleeding from the anterior ethmoid area. Here ligation of the anterior ethmoid artery was effective, and a relatively simple and safe procedure.

Heinberg[30] used an estrogenic substance in post-operative (tonsil and adenoid) hemorrhage in four cases, with excellent results.

Goldman,[31] in a series of forty-two patients with recurrent epistaxis without any form of blood dyscrasia, treated them with subcutaneous injections of moccasin-snake venom. No other adjuvant treatment was given. The venom therapy was effective in practically all instances either in completely arresting and controlling the nasal bleeding or in markedly diminishing its amount and frequency.

Scal[32] cured a case of severe nasal hemorrhage by radium application alone. Three hundred millicurie hours of radiation were used in each nostril.

COMMON COLD

Dochez[33] details the methods employed to isolate the virus of the common cold, to preserve and cultivate it, and to test its activity in human volunteers. Whalen[34] gives the routine for simple rapid examination of material from the ear, nose, throat, and lower respiratory tract that may harbor pathogenic fungi. He notes the similarity between the pulmonary lesions produced by the tubercle bacillus and by some of the pathogenic fungi, and suggests that the tubercle bacillus may be a yeastlike organism in some phase of its life cycle.

Montgomery[35] emphasizes the relation of climate to diseases of the upper respiratory tract. He feels that the incidence of head colds is definitely related to changes in humidity and temperature. He claims that climate is important in treatment, that the nose is a factor in maintaining the water balance of the body, and that the efficiency of its ciliary and other functions definitely depends upon changes in climate.

Sewall[36] stresses chronic sinusitis as being the endemic focus of the common cold. He maintains:

> The person with chronic sinusitis is the carrier of the common cold. Besides, in "false colds" to which chilling and indiscretions subject him, he is capable of originating within himself, independent of outside contacts, a true, infectious common cold. This is due to the fact that bacteria lurking constantly in his tissues gain potency when his immunity has expired, a true common cold resulting. He

is then capable of imparting his cold to others, either by a virus or otherwise, whether they have chronic sinusitis or not. Thus do epidemics of the common cold appear during the colder seasons, which fan into activity the many chronic infections of the sinuses. The person without chronic sinusitis takes "cold" only when the infection is carried to him by one with an acute cold. He never takes cold from chilling. The true cold confers a definite immunity for from six months to a year. The "false cold" is an exacerbation of a chronic sinusitis and confers no immunity.

Use of sulfur dioxide in the treatment of colds is suggested by Rawlins.[37] He found that in what was apparently an epidemic of colds, sulfur dioxide gas inhaled in the first twelve hours of the disease stopped the cold in twenty-four hours in a large percentage of cases.

Instillation of various chemicals into the nose to prevent absorption of viruses and organisms has been tried in the past with poor results. Rake[38] observed that Prussian blue particles pass rapidly from the surface of the olfactory mucosa and within two minutes are found in the tissue spaces, in blood and lymph vessels, in the perineural spaces of the olfactory nerve fibers, and in the subarachnoid space and pia-arachnoid membrane. Preliminary treatment of the olfactory mucosa with tannic acid does not alter the speed of absorption. It does, however, cause an inflammation of the mucosa, and appears to prevent the pigment from entering the olfactory sensory cells. Both pneumococci and *Salmonella enteritidis* pass through the olfactory mucosa and reach the tissue spaces, the vessels and the subarachnoid space with the same rapidity as the pigment. They invade by passage between the cells of the mucosa, and there is no apparent affinity of the organisms for the olfactory sensory cells. Tannic acid treatment of the olfactory mucosa in no way alters this invasion of organisms through the mucosa. The pantropic virus, equine encephalomyelitis, was detected in the fore-brain as promptly as were pigment and bacteria; neurotropic viruses, on the other hand —those of St. Louis encephalitis, rabies and louping ill—were not demonstrated in less than twenty-four hours.

Armstrong and Harrison[39] found that the instillation of various chemicals into the nostrils of mice and monkeys tended to prevent intranasal infection with the virus of the St. Louis type of encephalitis and of the monkeys with the virus of poliomyelitis. Trinitrophenol in concentrations of from 0.32 to 0.64 per cent, either alone or combined with alum, was found to be superior to four per cent alum and to be the most satisfactory and efficient experimental agent so far tried by the writers. Trinitrophenol in the concentration and amounts employed was devoid of detectable general or local injurious effects on animals.

NASAL SINUSES

That the development of the nasal sinuses normally occurs by means of a pneumatizing power of the nasal mucous membrane similar to the development of the temporal bone is brought out by Richter.[10]

Richards[11] has devised an apparatus to make repeated measurable observations of the results of transillumination of the maxillary sinus. By means of a photolectric cell it is possible to measure accurately and make a permanent record of trans-illumination of the maxillary sinus. This enables one to follow the clinical progress of any given case without repeated x-rays.

In most cases of antral disease the diagnosis can be made with certainty by direct inspection of the nasal cavity, simple x-ray examination, and proof puncture. Sometimes, however, proof puncture gives a negative result, yet the x-ray picture shows a shadow the pathological significance of which may be doubtful. Again, it may happen that the symptoms point to antral disease, while ordinary methods of examination disclose nothing abnormal. In such cases any many others, further information may be obtained by x-ray examination after contrast filling. Kettel[12] introduces the fluid by direct injection. He has examined in this way 100 antrums, the result in each case being verified afterward by operation.

Chronic sinusitis is a common infection in children. Marks[13] considers it one of the major problems in pediatric practice because of its high incidence and its various sequelae. The treatment of chronic sinus disease depends not only on the improvement of drainage from an infected sinus but on the intelligent observance of principles of management applying to a child with any chronic illness. The early recognition of the signs and symptoms of chronic sinus infection and the prompt treatment of this disease syndrome do much to lessen the severity of the illness and the frequency of its complications.

The relation of bronchiectasis to chronic sinus disease is a subject of controversy. Larsell[14] has investigated the lymphatic pathways from the nose. He finds four routes by which material in solution or suspension can reach the bronchial and mediastinal lymph nodes from the region of the paranasal sinuses. These are (1) the trachea, (2) the combined path of the lymph nodes, tracheal lymph duct and blood vessels through the right side of the heart and the pulmonary bed, (3) the purely hematogenous path, and (4) lymph spaces and channels in the visceral cervical space, the dorsal wall of the esopha-

gus, the prevertebral fascia, and related structures, which communicate with the anterior part of the mediastinum. The pathways by which the trypan blue reached the chest from the paranasal sinuses and from the posterior portion of the nasopharynx he describes in detail.

Patients with fever of obscure or "unknown" etiology, especially those with headache, should as a matter of routine have a roentgenographic examination of the paranasal sinuses, intranasal examination, and diagnostic irrigation of the sinuses. Sohval and Som[45] established sinusitis as the cause of obscure fever in nine cases. The disease in the sinuses was masked in general by the absence of localizing symptoms on one hand and the presence of misleading constitutional manifestations on the other.

As is well known, the occurrence of a positive blood culture in a case of acute mastoiditis indicates the existence of a complication. This is also true in acute sinus disease, according to Goldman.[46] In a series of 300 cases he finds that, except for an occasional case, the occurrence of a positive blood culture in acute sinusitis points to the coexistence of a complication or some associated systemic infection. His explanation of this failure of acute paranasal sinusitis to develop bacteremia unless followed by complications is as follows:

> The veins that drain the mucous membrane of the paranasal sinuses and penetrate their bony cells may be so small that they become thrombosed and sealed off before organisms can enter the general circulation. When a focus is set up in the skull, meninges or orbit by contiguous extension from a sinusitis, however, invasion of the blood stream may then occur from an infection of the larger veins which drain these sites. These veins, because of their larger size, do not thrombose so easily, and are able to feed the general circulation repeatedly with showers of bacterial emboli.

Kramer and Som[47] report ten cases of sphenoid sinusitis with meningitic symptoms, six of which terminated fatally. The authors discuss the symptoms, diagnosis and treatment of these cases. They believe that the intracranial involvement is predominant, and that the sphenoid sinus is likely to be overlooked as the basic lesion, and add that these cases are unlike those of uncomplicated sphenoid sinusitis.

Wattles[48] reports a case of benign giant-cell tumor of the ethmoid labyrinth. This is a rare disease, only seven cases having been previously reported.

Arons[49] emphasizes the benign character of an ossifying fibroma of the maxillary sinus. With an original diagnosis of osteosarcoma,

radium therapy was followed by x-ray. There has been no recurrence after ten years.

Mithoefer[50] discusses the non-operative treatment of sinus disease.

Fitzhugh[51] finds that neosynephrin hydrochloride produces constriction of longer duration than that caused by ephedrine hydrochloride, and that there are no apparent undesired effects.

The frequency of infection with the staphylococcus in sinusitis and early bronchiectasis is noted by Woodward.[52] He advocates treatment along specific lines with staphylococcus toxoid and antitoxin, in addition to the older, well-recognized methods.

Bryant[53] believes that fever therapy augments the vascular phase of inflammation and that it is of value in the treatment of acute sinusitis.

Van Alyea[54] has made a study in 164 cadavers of the surgical accessibility of the osteum of the maxillary sinus. In half of his specimens canalization of the osteum was impossible or very difficult, so that from a mechanical standpoint puncture is the more efficient method. He states that a cavity may be more rapidly and thoroughly flushed out when separate openings are used for intake and outflow.

Shea[55] and Miller[56] detail their operative procedure in establishing permanent openings into the antrum through the nasoantral wall.

A review of the published investigations on regeneration of sinus mucous membrane after operative removal has enabled Brownell[57] to say:

> From the microscopic and macroscopic observations described, one is drawn to the inevitable conclusion that complete regeneration of the lining of the paranasal sinuses, including ciliated columnar epithelium, is the rule after the operative removal of the original membrane. The time required for complete regeneration of the epithelium is apparently between three and five months. The type of cells composing the regenerated lining depends, in part at least, on its source, for while the epithelium is usually of stratified ciliated columnar type and comes from the nasal mucosa, it may be of stratified squamous type and come from the buccal mucosa.

Articles on the technique of radical surgery of the frontal and ethmoid have been written by Howarth,[58] Yates,[59] Sanson,[60] Reeves[61] and Hajek.[62]

OSTEOMYELITIS OF THE FRONTAL BONE

Because of its insidious onset, the paucity of external symptoms and its course, leading to brain abscess and death, osteomyelitis of the frontal bone is one of the most dreaded complications of infection of

the frontal sinus. In the past few years, following the lead of Furstenberk and Mosher, real progress has been made in combating and overcoming this disease. Its pathology, bacteriology, symptoms, signs and treatment are becoming better understood. During the past year papers have been published by Mosher,[93] Fincher,[64] Jones,[65] Williams and Heilman,[66] Behrens,[67] Adson and Hempstead[68] and Lemon.[69]

The predominating organism has been found to be *Staphylococcus aureus*. But it may be found with increased use of anaerobic cultures that this is not the true etiologic agent. Williams and Heilman[66] says:

> The finding of the identical organism, an anaerobic streptococcus, in two cases of osteomyelitis of the frontal bone, together with the apparently unusually favorable results obtained by specific therapy with an autogenous antivirus, is suggestive that the organism causative of this lesion may have been isolated. This hope is intensified by the fact that previously there has not been any adequate explanation as to why in an occasional case of frontal sinusitis this lesion should develop either spontaneously or after operation, when the bone is equally exposed to infection after any type of infection of a sinus or intervention which involves it. The conjecture that the disease is of staphylococcic origin has not seemed satisfactory, because staphylococci are frequently present in sinuses which have been operated on without producing this type of pathologic change. We present our findings with the hope that they will be confirmed in further investigations by ourselves and by others. Treatment with the antivirus clinically seemed to have a favorable effect in these two cases.

The mortality rate, however, is high. Lemon,[69] in reviewing 91 cases of osteomyelitis of the frontal bone, found the mortality to be 51.6 per cent; of these deaths, 55 per cent followed an acute infection and 45 per cent a chronic infection. Brain abscess was a complication in 30 per cent of the 91 cases.

It may be, as Behrens[67] suggests, that there are two types of cases, the localized or self-limited type, and the progressive type, but the latter is the one usually seen in this part of the country. It is this type that demands radical surgery, which must be prompt and thorough. All surgeons, of course, stress the value of supportive measures. Blood transfusions, bacteriophage and vaccines are to be used throughout the course of the disease. But conservative measures alone are inadequate. Radical operation—multiple radical operations if necessary—offers the best chance of success.

Mosher has outlined a clear, orderly, logical method of procedure in these cases. His work is firmly supported by pathological study. In his latest paper[93] he concludes:

> In reviewing all the cases which we have had at the Infirmary, especially those of the past five years, our operative results have been progressively better, and better in direct proportion as the operations performed were systematic and radical.

I feel even more strongly than I did in my original paper of three years ago that the edema of the skin of the forehead is a rough guide to the extent of the bone and periosteal infection. Further, as was pointed out in that paper, if there is actual bone necrosis the bone is infected without necrosis for an inch to an inch and a half beyond the necrotic area. Bone necrosis does not occur until seven to ten days after the pitting edema appears, and the x-ray is not positive until necrosis appears. Examination of the bone specimen removed in two of the cases just reported showed that the infection spreads along the inner surface of the bone, as well as by the diploic veins. When the infection spreads by way of a diploic vein it may localize at a point far from the original source of infection. When it does so localize, the pus tends to work both inward and outward, giving either a subperiosteal abscess or an extradural abscess, or both, with a destruction of the bone between the two. When a case has lasted two or three weeks, the operator should expect to find one or both of these conditions.

The more I see of osteomyelitis of the frontal bone, the more I feel that the whole face of the frontal bone should be removed as a routine from the hairline to the eyebrow. Preferably, it should be removed in one piece. However, if the patient is in poor condition and there is an area of necrosis, it is justifiable to work from the necrotic area outward, removing the bone for an inch to an inch and a half in all directions from the necrotic area. I believe further that both frontal sinuses should be opened, and the anterior and posterior walls of each sinus removed. I feel strongly that the lateral limit of the bone flap on each side should be at least the outer angle of each frontal sinus, or better, the outer angular process of the frontal bone on each side. The objection to this extensive removal is the deformity. It has been proved that fully 90 per cent of this can be corrected by modern plastic surgery. Therefore the surgeon should not allow his hand to be halted by the question of deformity. If he does, he will lose most of his cases of osteomyelitis of the skull.

HAY FEVER

Coke[70] describes methods by which cases of paroxysmal sneezing can be separated into allergic groups: microbic groups and those which are primarily of vasomotor origin. Suitable treatment is suggested for each group.

Clarek and Rogers[71] regard allergic rhinitis as the initial and simplest form of a general allergic disease of the respiratory tract, occurring equally in the two sexes. Allergic rhinitis responds well to allergic treatment. For some reason these authors find that men are more likely to have the more serious forms of the disease—asthma and hay fever.

According to Linton,[72] intramucosal tests are superior to intradermal tests in allergic rhinitis. He finds that the reactions to intradermal tests are not a reliable index of the sensitivity of the nasal mucous membrane. The offending allergens, however, in most persons with negative cutaneous reactions can be determined by intramucosal tests.

There is lack of agreement as to the nature of the active substances of pollens; some experimenters believe them to be albumins, while others think that they are of small molecular structure. Benjamins[73] concludes from his experimental work that the active substance of pollen is not a protein but a small molecular substance.

The importance of molds in seasonal hay fever and asthma is brought out by Feinberg.[74] His conclusions are as follows:

1. The ever present spores of fungi in the air are common causes of respiratory allergy.

2. A great tendency exists for many of the mold-sensitive patients to assume a seasonal character in their symptomatology because of the greater prevalence of mold spores in the warm months.

3. The evidence for the etiologic factor of molds in the group discussed consists of positive skin and passive transfer tests, the history of a "season" which is not in entire conformity with the pollen reactions, the clinical observation of the patients and comparison of their symptoms with reference to daily pollen and mold counts, the failures in pollen treatment, and the good results and a few systemic reactions with mold desensitization.

4. This group consists of such a definite unit that with some experience most of these patients can be catalogued before sensitization tests are made.

5. Of twenty-eight patients treated by specific mold desensitization and observed during at least one season, twenty-three obtained satisfactory results.

6. The conclusion cannot be escaped that seasonal hay fever and asthma due to molds is a definite and important allergic entity, second in importance only to pollen disease.

Zinc ionization (iontophoresis) has not yet established its true place as a form of treatment. Harkness[75] explains why he does not as yet use iontophoresis. This, he says, is a local symptomatologic treatment, perhaps a form of cauterization. The symptomatology is definite and the procedure simple. Facilities for interpreting results are easy. Individual technique should not be a material factor. But the author cites reports from the current medical literature, and offers a strong protest because according to it the relief obtained varies from zero to 100 per cent. He adds that as regards the harm that may be done, the various methods of carrying out the treatment, and so forth, there is similar disagreement.

Dean[76] states definitely:

Ionization does improve most cases of allergic rhinitis. The less the sensitivity to allergens, the greater the relief. Ionization does produce deleterious results in the mucous membrane of the nose which last at least two years. Many changes are permanent.

There is no excuse for using ionization if procedures that do not produce deleterious results will give a satisfactory result. Ionization should not be used unless the benefits derived are greater than the deleterious results produced.

Jarvis[77] stresses the use of suprarenal concentrate in otolaryngology. He finds it of value in treating edema of unknown etiology, urticaria, angio-neurotic edema and hay fever.

Scott-Brown[78] discusses the technique and use of radium in recurrent polyps of the allergic type. He achieved "dramatic" results in fourteen cases.

OZENA

The etiology and treatment of this disease remain unsolved problems. Kurata[79] carried out experiments in rats that enabled him to conclude that it is a deficiency disease due to lack of vitamins and sunlight. The specific symptoms appear at puberty, owing to rapid development of the "sympathicoendocrine" glands. Reichardt[80] reviews the literature on the problem of inheritance of ozena, and reports studies in 27 families in which the disease occurred. He thinks that the condition is inherited as a dominant mendelian characteristic.

Amersbach[81] gives his views on the pathology and treatment of ozena, based on twenty years' experience. During this time he treated some 400 cases, and most of them were followed up for long periods. The genuine forms of atrophic rhinitis, he states, must be clearly distinguished from the secondary forms, for example, those in tertiary syphilis, and after severe trauma of the nose. The theory that ozena is caused by chronic sinus suppuration has lost support. Such forms of atrophic rhinitis are often associated with a sclerosis of the face bones and a poor development of the accessory sinuses. This change in the bones is not secondary to ozena, but is due to an interference with free pneumatization, a function of the mucous membrane. There is a constitutional inferiority *(Minderwertigkeit)* of the mucous membrane which is the cause of both atrophic rhinitis and of the poorly developed sinuses. Amersbach explains the pathology in the same way as that of the sclerosed mastoid in chronic middle-ear suppuration. The term "sclerosing ozena" is, he holds, a misnomer.

He states that the various theories which attribute ozena to endocrine influences, or which have linked the etiology with certain chemical states of the blood, such as cholesterin deficiency, alteration of the calcium level, and so forth, have not withstood subsequent critical analysis. Specific infection theories (Perez, Abel-Lowenberg) are also being gradually abandoned, and with them vaccine therapy.

Lautenschlager's operation for ozena consists in mobilizing the lateral nasal wall and pushing it toward the septum. The good results,

he believes, are entirely due to the extensive formation of granulations and the temporary increase in the circulation of the part, associated with the operative trauma. The more the outer wall is broken up during the operation, the better the result. The relief from symptoms is only temporary, and they have usually returned when the patients are seen again in after years. The same arguments, in Amersbach's opinion, apply to the various implantation proceedings. A wide nasal cavity per se is not a causative factor in atrophic rhinitis. Many persons have wide noses with a normal mucosa.

Zakrzewski and Wiza[82] found bacteriophage therapy good in controlling the disease, but noted relapses in all of thirteen cases a few weeks after cessation of treatment. Colloidal manganese, administered intramuscularly and by mouth, was used by Mörch.[83] He examined twenty-five patients at periods of from one to seven and a half years after their courses of injection, and found permanent disappearance in fourteen cases. There had been temporary success in eight others.

Stovin[84] has found galvanic current an excellent form of treatment. He says:

> The stimulation of the mucous membrane produced by the galvanic current tends to restore its normal physiologic function. In most cases of ozena, the loss of the foul odor after this procedure is striking. In simple atrophic rhinitis a notable result is the restoration of the sense of smell. This treatment of course does not narrow the nasal cavities, but it restores the membranes to a healthier appearance and improves the sense of smell.

MOUTH

Lesions of the tongue, lips, gums and palate occur frequently, and are the forerunners of a serious condition known as alcoholic pellagra, which is probably a deficiency disease. The term stomatitis in general covers the condition. The mucous membranes become deeply reddened, swollen and tender, and here and there ulcers of a mild type develop. Vincent's organisms are easily demonstrated. In a series of over 200 patients suffering from chronic alcoholic pellagra, 60 per cent were found by Blankenhorn and Spies,[85] to have these lesions of the mouth and tongue. According to these authors early treatments consisting of a nutritious diet, wheat germ, and extracts of yeast and liver result in marked improvement in from twenty-four to thirty-six hours, and within a few days the tongue and mucous membranes have returned to their normal condition.

The five steps in treatment of carcinoma of the lip stressed by Hollander[86] are these: (1) establishment of the diagnosis through examination of the local lesion and serologic tests of the patient to

exclude syphilis; (2) correction of oral sepsis; (3) treatment of the local lesion with unfiltered roentgen rays, in massive doses to produce blistering; (4) treatment of the cervical lymph nodes, whether palpable or not, with heavily filtered deep radiation; (5) aftercare, including careful follow-up to make sure that the patient does not return to the use of tobacco and to habits of poor oral hygiene, examination of the lymph nodes and periodic blood counts.

It should be emphasized that 98 per cent of all cancers within the buccal cavity or on the lips are said to occur in individuals who neglect their mouths. In the last five years cancer of the mouth in white women has increased 45 per cent in Georgia, possibly because of the increase in cigarette-smoking. Campbell[87] concludes: "Cancer of the mouth is hard to cure but is easily prevented by proper care of the teeth, avoidance of excess use of tobacco, and prompt treatment of leukoplakia and chronic irritations of the tongue or lips."

Ward and Betts[88] use radium capsules in epitheliomas of the lip, and follow this with fairly heavy x-ray treatment, only applied to the neck if there is definite evidence of metastasis.

The relief of pain during irradiation treatment of oral cancers can be secured by alcohol injections of the second and third divisions of the fifth nerve. This allows the patient to wear the necessary protective shield more comfortably, makes cleansing of the mouth easier, and permits better nutrition during the period of increased radon reaction. The technique of injection is described in detail by Hare, Poppen and Hoover.[89] The second division of the fifth nerve is injected for lesions which involve the hard palate and anterior three-fourths of the soft palate, the maxilla and the upper portion of the cheek. They inject the third division for lesions of the tongue, the floor of the mouth, mandible and lower portion of the cheek.

True aberrant goiter in any location is seldom observed. Rosedale[90] reports a case of the "tongue root" type of intralingual thyroid presenting far anteriorly in the tongue, together with the results of its assay for iodine and a detailed description of its gross and microscopic pathology.

The incidence, pathology, signs and symptoms, complications and treatment of intralingual thyroids will now be discussed in relation to some of the pertinent literature.

Buckman's[91] conclusions are as follows:

1. Lingual thyroid tumor is a developmental abnormality presenting at the base of the tongue, or within or beneath the tongue, resulting from a vestigal rest of the thyroid anlage.

2. The precaution should be made of ascertaining the presence or absence of other thyroid tissue in the normal location before removing the lingual growth for the relief of symptoms.

3. The lingual tumor may produce grave dyspnea, dysphagia or hemorrhage, but is unlikely to undergo malignant change.

4. It usually appears in the female, at the several periods of endocrinal hyperactivity; puberty, pregnancy and the menopause.

5. Removal of the lingual thyroid may be, and often has been, followed by myxedema. The postoperative appearance of tetany has been reported, and points to the association in development between the thyroid gland and the parathyroid.

Laryngeal thyroid is extremely rare, as rests of thyroid tissue there are outside of the usual course of embryonal descent. Beeson[92] reports a case of aberrant intralaryngeal thyroid tumor, with recovery and non-recurrence, in a man fifty-one years old.

Lipoma of the tongue is very rare. Mazzini states that only one case occurred among 259,366 patients seen during thirty-one years. There are forty-four authentic cases in the literature, to which a case reported by Smith[93] is to be added. A forty-five-year-old woman had a lipoma of seventeen years' duration removed by him. The histologic report was "simple lipoma." The mass weighed 32 gm. and measured 11 by 9 by 7 cm. This is the largest of these tumors to be reported.

Spencer[94] reviews the literature and reports fourteen cases of advanced carcinoma of the tongue. The patient who survived operation the longest lived three years, four months and nineteen days. He feels from a review of the literature that definite progress is being made in the treatment. The disease is recognized earlier. Broders' classification is a real help in outlining treatment. Surgical diathermy has been a definite improvement over cautery, although it has not displaced cautery entirely, and should not. Irradiation by high-voltage roentgen rays is an improvement over low-voltage irradiation, just as the radium bomb or teleoradium is an improvement over the use of small quantities of radium. The recognition of the importance of syphilis of the tongue in causing cancer of carious teeth with poor dental hygiene he believes will do much to prevent and relieve the suffering from lingual carcinoma.

SALIVARY GLANDS

Congenital absence of salivary glands is evidently a rare abnormality. Cases of absence of the submaxillary glands alone have been reported by Gruber in 1885 and Bruno in 1894. Nayak in 1926 published a case of congenital absence of the parotid glands, and

Ramsey has reported absence of salivary secretion in a father and daughter both suffering from dental caries.

A case of congenital dysfunction of the salivary glands is reported by Sharp.[95] These were present but atrophic. Dental caries and atrophy of the mucous membrane of the mouth and tongue were observed, as in all previously reported cases. No abnormality of the lachrymal apparatus was detected apart from the fact that the boy was never seen to shed tears. There was no hereditary factor in the case. The boy was eight years old, and the remainder of his examination was essentially negative.

A case of Mikulicz's disease is reported in very great detail by Aboulker.[96] His conclusion, which is backed by a biopsy of the parotid gland, is that Mikulicz's disease is a cirrhosis of the lachrymo-salivary system. It is a dystrophy of unknown cause not unlike certain hepatic cirrhoses the origin of which cannot be accurately determined. Prognosis in these cases is not bad, but treatment must be prompt and thorough. The most satisfactory form of treatment is radiotherapy. By this means the lymphoconjunctival neoformation is absorbed, and this allows that part of the gland which is still alive its liberty of function.

The facts that parotitis is relatively common and that calculi in the parotid are relatively rare, whereas the opposite obtains in respect to the submaxillary gland, are well known. The reason for this is probably the difference in the secretions of these glands. That of the parotid is poor in mucin, whereas the submaxillary saliva is rich in mucin. The fact that mucin readily dissolves mineral salts and is strongly bactericidal probably accounts for this.

Ruppe, Lattès and Voisin[97] present five cases of parotid lithiasis. They state that the disease may occur at any age, manifesting itself by swelling and pain, and sometimes leads to suppuration. Abscesses which occur in connection with Stenson's duct anterior to the masseter are the most favorable, as these often discharge into the mouth. Those occurring more posteriorly in the gland may lead to a salivary fistula and are best treated by radiotherapy. They believe that diagnosis with lipiodol helps to differentiate intermittent partitis, cysts of Stenson's duct and parotid abscess.

The value of lipiodol should be emphasized; it has enabled us to make great progress in our diagnosis of salivary gland disorders. For this reason, Csillag's conclusions[98] in regard to the use of a radio-opaque medium are here quoted in full:

In addition to calculi, which have hitherto been regarded as the most frequent cause of intermittent swelling of the salivary glands, account must be taken of obstruction due to pathological changes in the ducts themselves. Acute inflammation of the glands, as in mumps, is sometimes followed by connective tissue thickening (fibrosis), with strictures of the ducts. Inflammatory diseases of the mouth may lead to catarrh of the salivary ducts, with swelling of their mucous membrane, and thick secretion which blocks the already narrow lumen. There may thus be formed localized dilatations of the ducts (sialodochitis cystica), which tend to become more numerous and larger the more often the inflammatory attacks (parotitis intermittens acuta) are repeated.

The diagnosis of these conditions has been rendered possible by x-ray examination with "contrast filling" (sialoadenography), and there remain few cases of swelling of the salivary glands the cause of which cannot be determined by this means, together with clinical examination (for example, the use of a sound).

This author reports eight cases (six women and two men) of intermittent salivary gland swelling, in four of which obstruction by calculus could be excluded by contrast filling with lipiodol and sialoadenography which showed that the salivary passages were free from obstruction, and the diagnosis of regional lymphadenitis, probably of tonsillar origin, was thus confirmed. In the four other cases the sialoadenogram showed widening of the ducts and ectasia of the smallest canals, so that the x-ray picture suggested a cluster of grapes. There was reason to suppose that in each of these cases the condition was the result of patches of cicatricial thickening in the duct system, originally due to epidemic parotitis. "Contrast-filling with lipiodol," he says, "was of practical value not only in the diagnosis, but also in the treatment of those patients in whom there was disease of the ducts or glands."

Adenoma of the parotid is relatively rare—so rare, indeed, that its occurrence has been doubted. However, since the question of its validity was raised twenty-odd years ago some fifteen cases have been recorded, to which Kunstmann[99] adds four of his own. He recognizes an acinous and a canalicular type. The former arises in the glandular portion of the parotid, is lobular in outline and encapsulated, and, like the parotid of the newborn, secretes mucus, though this feature has received but little attention in previous descriptions. Adenomas of the canalicular group, to which three of his cases belonged, are neither lobular nor encapsulated, and are distinguished by a profuse secretion of mucus with extensive cyst formation and papillary outgrowth. They originate in solid undifferentiated buds from the ducts, and sometimes consist rather of large alveoli. Carcinomatous change has not yet been encountered. He adds that the few solid adenomas reported in the literature probably belong in the acinous class, though the possibility that there exists a pure, solid, canalicular adenoma cannot be dismissed.

Harris[100] describes a tumor at the angle of the right jaw in a man of seventy, which was removed with the parotid gland. He believes this to have been a parotid gland adenoma arising from the duct cells. It closely resembled the tumor reported by Gruenfeld and Jorstad[154] and described by them as an onkocyte tumor.

The occurrence of pulmonary metastases from tumors of the mixed salivary group is not rare, as evidenced by the report of three consecutive cases by Olson.[101] He feels that the clinical and pathological study of these tumors is of little prognostic value because the degree of malignancy cannot be accurately determined, and advocates routine roentgen studies of the chest before therapeutic measures are undertaken.

TONSIL

Minear, Arey and Milton[102] have made an interesting study of the development and form of the crypts of the palatine tonsil. Their findings are as follows:

> The crypts of the human palatine tonsil begin to appear during the third fetal month as solid ingrowths from the epithelial wall of the tonsillar fossa. Subsequently these epithelial processes grow, branch and canalize, although the end of such progressive development is not reached until late childhood.
>
> Although the maximum number of crypts is reached during childhood, these later elongate and enlarge by interstitial growth to form the definite crypt system.
>
> The approximate area of the epithelial lining of the adult crypt system of one tonsil was calculated to be 46 square inches (295 square centimeters), whereas the exposed surface area of an entire pharynx was only 7 square inches (45 square centimeters).
>
> Any tendency to empty the tonsillar crypts through natural or artificial means must necessarily be highly inefficient, owing to anatomic constrictions and the tendency of the contents of a complex convergent system to impact at the bottle-neck region of the main crypt. Such plugging is further enhanced by the circumstance that the main drainage channel is often smaller than its tributaries.

Histopathologic studies of the tonsil by Meeker[103] bring him to the conclusion that mucous glands open into crypts and are closely related to tonsillar lesions, such as peritonsillar abscesses. He thinks that the true lymphoid tissue found beneath the main tonsillar mass in the adult is an extension along mucous glands (not along blood vessels). The recurrent tonsil in the adult arises from residual tissue about the mucous glands. He finds a constantly recurring group of mucous glands associated with a bar of cartilage. These are always in the same location, in the constriction between the middle and lower lobes of the tonsil.

Urbantschitsch[104] histologically examined the tonsils and adenoids of 446 patients. All specimens examined showed alterations

due to chronic inflammation. In seven cases deposits of lime salts were seen, and in thirty-three extensive fugus colonies. Epithelioid cell tubercles were present in five cases (the adenoids were affected in two) where there was no evidence of a general infection or any suspicion of tuberculosis macroscopically. In two cases (a man, aged thirty-five, and a girl, aged ten), a carcinoma was proved to be present in the tonsils. Macroscopically the tonsils were of similar size and showed no external evidence of neoplasm. In both patients the chemical blood test (Freund-Kaminer) was positive.

Seventy-five pairs of tonsils removed by tonsillectomy were examined by Menzel[105] both histologically and bacteriologically. Professor Lowenstein obtained tubercle bacilli in pure culture from the tonsillar tissue in five cases. Histologically, definite tubercle formation was found in only one case, which incidentally belonged to the series from which positive cultures were obtained. He states that in all probability there is a generalized tuberculous infection of the body which results on the one hand in the presence of bacilli in the tonsils, and on the other in a joint rheumatism exhibiting an allergic phase of the infection, in-so-far as in all cases positive lung findings were obtained.

Smith[106] presents a correlation of the history leading to the tonsillectomy, the pathological diagnosis of the tonsils and the subsequent clinical course over a period of eight months. From this study it appears that in a routine group of patients the percentage of persons who give evidence by history or clinical examination of infected tonsils should be between 85 and 90. In this series the microscopic examination of the slides revealed that 86 per cent had tonsils with a pathologic change. He continues that tonsillectomy and adenoidectomy have proved beneficial in cases in which a focus of infection was suspected in the tonsils and in which there was a history of recurrent colds and sore throats, aural involvement, nasal obstruction, cervical adenitis and enlarged tonsils. The procedure seems to be of questionable value in cases of indigestion, laryngitis and pain in the throat. The so-called immediate results of tonsillectomy, as noted in this study, are compared with the less favorable results after a period of ten years, as shown by the figures of Kaiser.

Acute rheumatism is usually caused by a streptococcal infection, according to Barwell,[107] and the source of the infection is in the lymphoid tissue of the throat. Its incidence is certainly diminished by tonsillectomy. Owing to the numerous scattered nodules of lymphoid tissue in the pharynx, however, tonsillectomy is not certain in its prevention, although it makes recurrence less probable.

Of 1112 patients with hay fever and asthma, Waldbott and his associates[108] performed tonsillectomy in 228 before the onset of allergic symptoms and in 205 after they had developed. In the latter group, tonsillectomy resulted in 1.9 per cent and aggravation of the allergic symptoms in 11.6 per cent. In a control group of sixty patients in whom tonsillectomy was performed after they had been under the author's care, the results were substantially the same. Tonsillectomy performed for conditions other than allergy was successful in 35.2 per cent of the allergic group, in 36.4 per cent of the "preallergic" group, as compared with 72 per cent improvement recorded in normal controls (Kaiser). In the 228 patients in whom tonsillectomy was performed before the onset of allergic symptoms, 14.4 per cent developed allergic manifestations within three months, 29.3 per cent within six months, and 48.6 per cent within two years after operation. This compares with 26 per cent showing frankly allergic symptoms within three months, 47 per cent within six months and 63 per cent within two years in patients whose tonsils were removed for the relief of "nasal colds" and "bronchitis." The greatest benefit from tonsillectomy was obtained in the earlier age groups. The operation was practically always a failure in patients more than twenty-five years old. The efficacy of the technique of removal did not affect the result. The operation was less successful when performed during the pollen season. Although the results of tonsillectomy were disappointing, these authors believe that it should be performed in patients having frequent infections. In others with allergic catarrh of the upper part of the respiratory tract which may or may not involve the tonsils, they believe that tonsillar tissue is a definite asset to the system and should be perserved.

Jackson, Parker and Brues[109] found twenty-eight, or 11.8 per cent, of 236 cases of malignant disease of the tonsil to be malignant lymphomas of one type or another. Nine additional cases from other sources are included in their study. The greatest incidence was in the seventh decade; and 62 per cent of the cases occurred between the ages of forty and sixty-nine. Five patients were in the second decade. The sex incidence was 57 per cent in males, 43 per cent in females. Sore throat was the commonest initial symptom, occurring in fourteen cases; enlargement of the cervical nodes (eleven cases) and swelling in the throat (six cases) were next in frequency. Subsequent symptoms developed rapidly, causing patients to seek medical aid in an average of four months from the onset of the first symptom. The tumor invariably had markedly enlarged the tonsil. In 67 per cent, either localized or generalized metastasis had occurred when the patient was first examined. The prognosis is poor, only eight patients

of this series being alive. Of these, one is alive after eighteen years, two after ten years and one after five years. The duration of life averaged two and a half years; it varies directly with the presence of localized or generalized metastases; namely, the more general the involvement, the worse the outlook. In 44 per cent of the patients who died, the disease was localized either to the tonsils or to the cervical nodes; in 56 per cent it had become generalized. The response to radiation is no index as to prognosis. They suggest that in the future the treatment should consist of very heavy initial radiation with comparable doses for recurrences.

Peritonsillar abscess has received considerable attention during the past year. Neffson and Brem[110] call attention to the fact that clinical diphtheria may sometimes be easily mistaken for it. This error often results in disaster. The harm done is due not only to delay in the administration of antitoxin but also to the fact that the patients are often subjected to incision of the peritonsillar tissues. Such procedures open up wide avenues for the spread of the infection and the absorption of the diphtheria toxin. Six patients, whose ages ranged between twenty-four and thirty-six and who had been subjected to peritonsillar incision, were observed over a five-year period. Three died of toxic myocarditis and other complications. Two of the surviving patients also showed evidence of toxic myocarditis. The high mortality rate and prolonged convalescence of the survivors are directly attributable to unnecessary surgical manipulation and delay in the administration of antitoxin. Whenever a patient with a supposed peritonsillar abscess is examined, diphtheria should be ruled out by repeated cultures. Incision of the peritonsillar tissues should not be done hastily. By following this conservative routine, they believe that the high mortality and the prolonged morbidity in this condition will be reduced.

True peritonsillar abscess (quinsy) in this part of the country is treated conservatively until localized fluctuation is present. Incision and drainage is then the procedure of choice. The results are excellent. Only rarely do we see a case of peritonsillar abscess in which the walled-off abscess forms at the base of the tonsil necessitating tonsillectomy for drainage. But Linck,[111, 112] Schroeder,[113] Thacker Neville[114] and Merica[115] advocate partial or complete tonsillar enucleation in the acute stage of peritonsillar abscess. Linck believes that there are often small collections of pus hidden away in the depths of the peritonsillar tissues which are drained by this procedure. With infrequent drainage such conditions may lead to thrombophlebitis of the large neck veins, an invasion of the blood stream and often a fatal

ending. The local signs in the throat are few and may be overlooked. He adds that abscess-tonsillectomy is the only certain way of opening and draining these dangerous hidden abscesses and that in peritonsillar abscess, primary abscess-tonsillectomy should be the operation of choice.

Schroeder, in presenting fifty-six cases, says that partial or total tonsillectomy, in order to get the pus as soon as possible, has yielded very good results, and that it is not proved that the procedure gives a less satisfactory post-operative course than incision. He states: "It is remarkable how many cases of peritonsillar inflammation are complicated by parapharyngeal abscess."

Merica has had no complications in twenty-one cases in which tonsillectomy was performed for quinsy and each patient showed immediate improvement.

In the ordinary case, however, this form of treatment seems to the reviewers more radical than necessary, and until it proves its merits should be left to the rare type of peritonsillar abscess which localizes at the tonsil base. It is to be emphasized, furthermore, that fatalities from unrecognized deep pus in the neck, secondary to tonsillitis and peritonsillar abscess, are continually occurring. The parapharyngeal or pharyngomaxillary space is the common site for accumulation of pus. Early adequate drainage must be done externally. The great vessels of the neck easily become involved. Boemer[116] emphasizes this point and Schroeder[117] describes the anatomic factors which explain the migration of pus in this area, outlining the surgical treatment of the condition involved. Infection from the tonsil occasionally spreads to the cavernous sinus by one or more of several routes. It may reach the internal jugular vein by the pharyngeal veins and then by the posterior route, passing by the inferior and superior petrosal sinuses to the cavernous sinus. On the other hand, it may pass from the jugular vein by the anterior route, through the facial, angular and ophthalmic veins to the sinus. A third route, he says, is by the pterygoid plexus and the vein through the foramen ovale to the sinus.

Tavani[118] reports a fatal case of cavernous sinus thrombosis following acute tonsillitis. Jauerneck[119] reports a case that recovered after operation on the ethmoids to relieve tension in the orbits; the sight of one eye was lost, however. Grove[120] reviews the literature on cavernous sinus thrombosis. His conclusions are as follows:

> There are septic and aseptic types of thrombosis of the cavernous sinus. The aseptic types are caused by penetrating injuries involving the sinus, by accidental injury to the sinus during an operation in its neighborhood and by fracture of the

skull and injury to the head. In this group must also be included the marasmic types of thrombosis.

In the septic types in which the thrombosis or thrombophlebitis reaches the cavernous sinus by way of its afferent vessels the mortality is practically 100 per cent.

In those cases in which the condition is septic and of the restrained or chronic compensatory type, in which the thrombotic process reaches the cavernous sinus by retrograde action along its efferent vessels, there is some hope of recovery. In the cases of this group in which recovery occurred the thrombotic process in the cavernous sinus itself must have been aseptic, although originating from a septic source elsewhere.

The percentage of recovery from all types of thrombosis of the cavernous sinus is probably not greater than 7 per cent. The percentage of recovery from the purely aseptic types is considerably higher than this.

Operations on the cavernous sinus have been extremely disappointing and have shown poorer results than non-operative treatment. When the thrombosis originates from a septic source the focus should be vigorously treated and eradicated. The cavernous sinus itself should be left alone. As an exception to this general statement, it would seem that ligation of the carotid artery, as proposed by Eagleton, might prove beneficial.

PHARYNX

After removal of the faucial tonsil there is a tendency in certain cases for the lateral pharyngeal bands to increase and to give rise to an unpleasant sensation. This may consist of sore throat, a sensation of a foreign body, or accumulation of mucus, causing swallowing or hawking. In such cases the topical application of remedies to the pharynx is disappointing. Lillie[121] has found that the ingestion of iodides gives good results, although he is unable to explain their action.

Schenck[122] studied histologic sections of tissue from the pharynges of 108 patients with systemic diseases and chronic pharyngitis. These invariably presented evidence of hyperplasia of the lymph nodules and chronic inflammation. In these patients the histopathologic changes were common to all the types of disease studied; no specific histopathologic characteristic differentiated the pharyngeal nodules of patients with one type of disease from those of patients of the other groups.

Brown[123] emphasizes focal infection resulting from the chain of lymph follicles in the lateral pharyngeal wall. He thinks that involvement of the lymphoid follicles or glands of the pharynx is rarely if ever a primary focus of infection. As a secondary focus it is a definite factor and source for the distribution of infections, and has long been overlooked or unrecognized as such. He believes that the elimination of this focus aids in preventing infections which originate

in the adenoids, tonsils, teeth and sinuses from being continued indefinitely.

Stout[124] reports the first case in the literature of dry-ice (carbon-dioxide ice) burn of the throat. Recovery was painful but otherwise uneventful.

Retropharyngeal abscess, commonly regarded as a condition of no special surgical risk, still carries an average mortality of 7.4 per cent, according to Richards.[125] Only its constant consideration as a possible explanation for a wide range of symptoms will prevent diagnostic errors. Careful digital palpation of the pharyngeal wall is preferable to the use of a tongue depressor or mouth gag; and pharyngeal incision, without anesthesia and in the prone position, will suffice to secure drainage in almost all cases. He adds that sudden severe hemorrhage must at once be controlled by carotid ligation. Schall[126] reports a case of an aberrant vessel of the posterior pharyngeal wall that ruptured four days postoperatively following evacuation of a hematoma which simulated a retropharyngeal abscess. Ligation of the common carotid artery stopped the bleeding, which was temporarily controlled by pressure in the nasopharynx and compression of the common carotid artery. Four months previously a retropharyngeal abscess in this location had been incised and drained.

Tumors of the pharynx, says Pilcher,[127] can be divided into two groups: (1) epilaryngeal, occurring almost exclusively in men; (2) postcricoid, seen almost exclusively in women and about ten years earlier than in men. In the epipharyngeal group, the commonest early symptom is a persistent abnormal sensation in the throat, varying in kind. Other early manifestations are enlarged nodes in the neck or interference with the voice. Postcricoid tumors are characterized by a long history of slight difficulty with deglutition; other symptoms are at first intermittent. A single serious attack of dysphasia in a patient with a long history of slight difficulty calls for a thorough examination. In the majority of cases, when symptoms first appear some abnormality can be seen by indirect laryngoscopy. These abnormalities are described. One hundred cases are analyzed; radical operations were completed in thirty-nine patients, with the death of sixteen and a survival of seven for periods of from eighteen months to ten years. He makes a plea for closer investigation of minor disturbances of the voice and of swallowing, with the use of indirect laryngoscopy in suspicious cases.

Albright[128] reports the case of a forty-nine-year-old man with a large tumor on the right side of the neck, of seven years' duration.

The growth protruded into the oropharynx, displacing the uvula upward and to the left. The overlying mucosa was intact. The firm, encapsulated growth, 8 cm. in diameter, was removed through a longitudinal incision in the neck. Histologic study showed it to be a fibroma, probably of perineural origin. The patient has remained well for two months after operation.

Torres and Monteiro[129] report a case of an unoperated upon retropharyngeal neurinoma in a man fifty years of age. The tumor, which had been growing slowly for about six years and measured some 6.5 by 4.5 cm., completely filled the retropharyngeal space. At autopsy a number of large cavities filled with pus were found; during life, arteriography and exploratory punctures had shown these spaces to be filled with blood. There was no metastasis.

Kanas[130] describes the case of a man forty-seven years of age with destructive ulceration which began on the posterior surface of the soft palate, and in a few weeks spread so as to involve the whole of the nasopharynx and a part of the pharynx. Secondary infection of the extensive, gangrenous, ulcerated surface was severe, and hemolytic staphylococci were found both locally and in blood cultures. No treatment was of any avail, and in about three and a half months from the beginning of the illness death followed hemorrhage from an eroded vessel. Microscopic examination of several specimens, removed during life, showed only ordinary granulation tissue. Further examination after death, however, showed that the disease was in reality an atypical lymphosarcoma.

In the Semon Lecture for 1936, Howarth[131] described cases of tumors and ulcerations of the palate and fauces. He outlined the technique of diathermy excision of malignant tumors which he has used during the last twenty years, and gave his results in sixty-one cases. After a brief review of the various forms of ulceration that are found in this region, he described a form of ulceration under the name of precancerous epithelioma and gave the histories of three cases.

NASOPHARYNX

Hill[132] stresses the fact that in malignant disease of the sinuses and nasopharynx certain common errors are encountered. One of these is failure to make a correct diagnosis through overlooking the nasopharynx as a possible site of the primary lesion, or through neglecting to have proper roentgenologic and pathological studies made. Another is a misguided zeal to preserve the cosmetic result at the expense of being sufficiently radical. Fortunately, both these faults may be easily remedied.

Flynn[133] reports a case of fibromyxosarcoma of the nasopharynx in a boy of twelve. This was removed and the boy has been well for nine years without recurrence.

A case of plasma cell tumor of the nose and nasopharynx is reported by Blumenfeld.[134] According to the author, who reports the abstracts of previous cases, this is the twenty-first case presented in the literature.

CYLINDROMAS

The name "cylindroma" is given to a numerous variety of tumors which differ in their clinical development, in the type of therapy required, and in their prognosis. The term ought to be abandoned, say Lemaitre, Ardoin and Lemaitre.[135] Tumors exist which are histologically cylindromatous but have few characteristics suggesting a common origin. Some are undoubtedly malignant tumors; on the other hand, others are relatively benign.

They add that the cylindromatous epitheliomas arise from seromucous glands, which are chiefly found in the upper digestive and respiratory tracts, the mouth, the pharynx (above all, the nasopharynx), the larynx and the trachea. They remain submucous for a long time, do not ulcerate, are slow-growing, show very little lymphatic spread, and never metastasize. They call for surgical removal, but often recur several months or years after operation, generally ending in death from seven to ten years later after three or four operative interventions; their degree of radiosensitivity has not yet been established. The cylindromatous precancerous states are commoner than the true cylindromatous epitheliomas, and their history is confused with that of the so-called "mixed tumors" of the salivary glands. Precancerous tumors are found, in order of frequency, in the parotid region, the arches and velum of the palate, and the submaxillary glands. Their development is slow and they have a good prognosis if completely removed, but their transformation into cancers is far from exceptional, and in this respect they differ from the mixed tumors. The cylindromatous epitheliomas of the skin resemble classical cutaneous epitheliomas, especially the basal-celled variety. Clinically, good results follow rational treatment—total excision.

Goldsmith and Ireland[136] report six cases of aberrant mixed tumors of salivary gland type. The general consensus is that these tumors are not true teratomas. Those closely associated with the glands proper probably arise from the gland ducts, and the aberrant type from embryonal rests. Cartilage and myxomatous tissue can be developed by metaplasia, and their mesodermal origin is not considered

essential. Tumors of this type involving the accessory sinuses are rare. One such case has been reported. The treatment by complete surgical removal was the most satisfactory measure in their series. Radiation as a primary treatment should not be considered; prophylactic postoperative radiation may have some usefulness. They add that recurrence of the growth is frequent, and make no attempt to report any of the cases as cures.

LARYNX

Tucker[137] reports an unusual congenital case of ptosis of the larynx in a child, due to replacement of the left sternohyoid and sternothyroid muscles by a tendinous band pulling the hyoid bone and the larynx downward. The result of the resection of the fibrous band has been satisfactory in overcoming the displacement. The child had a speech defect partly caused by interference with the proper use of the tongue by the displacement of the hyoid bone. Correction of the abnormality improved the speech.

Central lesions that produce paralysis of the larynx are discussed by Furstenberg.[138] Corticobulbar fibers carry motor impulses to the lower motor neurons which supply the larynx. Attention is first called to the pontine division of the aberrant pyramidal tract and the partial decussation of the corticobulbar fibers for the laryngeal group before they terminate in the nucleus ambiguus. Impulses brought to the recurrent nerves therefore arise in both the right and left precentral regions of the cerebrum, an anatomic fact of much importance when one is endeavoring to localize lesions causing laryngeal paralysis of central origin. Secondly, lesions above the nucleus ambiguus—the origin of the laryngeal nerves—cannot produce a unilateral paralysis of the larynx on account of the decussation of the corticobulbar fibers. When the lesion is large enough to involve them on both sides, a bilateral paralysis of a spastic type will be observed. Attention is called to a differentiation seldom made by the clinician, namely the spastic versus the flaccid type of laryngeal paralysis. Supranuclear lesions produce the former, nuclear and infranuclear lesions the latter. Thirdly, unilateral laryngeal paralysis of central origin is a not uncommon condition. It is seldom observed, however, because it is usually associated with a preponderance of obvious neurologic findings, which invite study and minimize the attention given to the special organs of the body. He adds that, in many cases of this kind, the symptoms are so trivial that neither the patient nor the doctor is aware of their presence.

Lore[139] and Sercer[140] present operative procedures for the relief of laryngeal stenosis due to bilateral abductor paralysis.

Hofer and Motloch[141] point out that membranous deformities of the vocal cords occur chiefly on the anterior commissure but occasionally on the posterior commissure of the cords. They vary in size from a slight web formation to complete atresia of the lumen. The genesis of these membranes has not been completely explained, but some authors regard them as embryonal remnants. They believe that the deformities are not necessarily congenital, for there are a number of disorders that may cause the formation of cicatricial membranes in the region of the glottis, namely syphilis, diphtheria, tuberculosis, typhoid perichondritis, leprosy, rhinoscleroma and glanders. These authors report a case in which tracheotomy and a bolt pushed up into the anterior commissure were necessary to obtain permanent cure. They state that chronic inflammatory tumors of the true vocal cords tend to increase in size because of the functional activities of the cords.

According to Tucker,[142] a vicious circle is set up in which local irritation, increase in the size of the tumor, and the overacting musculature of the larynx, all became important etiologic factors. Restoration of the normal contour of the cord by direct laryngoscopic removal of the tumors and by voice training to restore the normal muscular action will eliminate the vicious circle and restore the larynx to normal in most cases. The microscopic examination of the tissue removed by direct laryngoscopy provides a histologic basis for diagnosis.

Koch[143] gives the clinical histories of twenty-two cases of papilloma of the larynx treated by x-ray, and describes the exact dosage and methods of irradiation.

Palmer and Mehler[144] report a case of recurrent lipomyxochondrofibroma of the larynx operated on five times in five years.

Cummings[145] reports a case of lymphosarcoma of the larynx associated with skin manifestations and later with generalized fatal metastases.

Clerf and Bucher[146] write on blastomycosis of the larynx. Their conclusion is that in extensive inflammatory lesions of the organ with ulcerative and exudative changes which, although suggestive of tuberculosis, are not characteristic of any definite clinical entity, one should consider fungus infection as an etiologic possibility. In the three cases cited a tentative diagnosis of tuberculosis had been made. Repeated negative sputum studies for tubercle bacilli and negative pulmonary findings in spite of histologic diagnoses of chronic ulcerative laryngitis either granulomatous or suggestive of tuberculosis, indi-

cated a need for additional investigation. The final diagnosis rested on the results of the mycologic findings, together with the above-noted findings. Fungi were demonstrated in all the lesions. They produced definite lesions in rabbits. The positive mycologic findings at repeated studies and the improvement under iodide therapy were conclusive. In two other cases the findings were suggestive from a clinical standpoint. Although fungi were found in both cases, their pathogenicity was inconclusive.

A number of papers have appeared on tuberculosis of the larynx.

Schuster[147] studied the larynx from the clinical standpoint in 452 cases of pulmonary tuberculosis with subjective symptoms referable to the ear, nose or throat. Tuberculous laryngitis was present in 192; diseases of the nose and throat were no more frequent in these patients than in those in whom the diease was limited to the lungs. In this group only age, sex and pregnancy had any bearing on the development of tuberculous laryngitis. Tuberculous infection in the larynx usually comes from contact with bacteria-laden sputum, although it is probable that some cases, in which the sputum contains no bacilli, are lymphatic in origin. A strong local resistance to clinical invasion by the tubercle bacillus was noted in the upper respiratory tract, but no such immunity was observed for other infections.

He continues that reflected sunlight is occasionally of value in supervised cases. When the lesion is progressive, the radical and repeated use of the galvanocautery is of great worth, care always being taken not to exhaust the patient at any one sitting. Time and temporary relief may be gained by blocking the superior laryngeal nerve. The actual cautery is now well recognized as a most valuable aid, and he believes that its use has been too frequently reserved for patients with far-advanced and more or less hopeless conditions. Early use is urged, especially when the condition does not respond promptly to conservative treatment. He adds that the pathologic picture is essentially that of tuberculosis elsewhere and is extremely protean and that the diagnosis should be based on the gross observations in the larynx, with the confirmatory observations in the chest and the results of laboratory and roentgen study. Prognosis as to healing of the laryngeal lesion in the early stages is good, but uncertain as to ultimate recovery. Early treatment is based on co-operation in general care with the specialist in diseases of the lungs, on absolute rest of the voice, on pulmonary collapse in suitable cases and on avoiding over-treatment locally.

Blegvad[148] takes up the problem of early laryngeal tuberculosis. His article is based on 1773 cases suffering from laryngeal tuberculosis

that were treated in Copenhagen from 1916 to 1934. In 404 cases the final result is unknown, but of the remaining 1369 patients 74 per cent have died and 26 per cent are alive and well. The treatment has been that inaugurated by the Finsen Institute, namely universal carbon-arc-light baths or quartz-light baths. The patients are all ordered to keep silent. If there is no appreciable improvement within a few months, a local operation is carried out if the condition of the patient permits; it may consist of one or more of the following: galvano-cauterization, amputation of the epiglottis, excision of the affected part, injection of alcohol and resection of the superior laryngeal nerve. The author stresses the importance of early diagnosis, and emphasizes the following clinical diagnostic points: (1) isolated redness of the vocal cord; (2) swelling and redness of the vocal process; (3) prolapse of the ventricle of Morgagni; (4) swelling of the lower surfaces of the vocal cords; (5) swelling of the mucous membrane in the interarytenoid region; and (6) a red cushion beneath the commissure.

And we must not forget, as Hautant[149] emphasizes, that cancer may simulate tuberculosis and vice versa. Laryngeal tuberculosis can take the aspect of a warty, subglottic and unilateral lesion. Sometimes it resembles a ventricular tumor. In both instances the clinical aspect is that of an intralaryngeal epithelioma; a very careful examination is necessary to avoid an error. A radiograph of the larynx may be a valuable aid in the diagnosis of cancer. In doubtful cases, several biopsies should be carried out from different parts of the laryngeal lesion. Deep roentgenotherapy, even as a test treatment, should be resorted to only with great caution. He states that, even in cases in which a diagnosis of epithelioma seems obvious, a pulmonary examination and x-ray should always be made and taken into consideration.

Rubaltelli[150] reviews the literature and states that the results obtained with either periarterial sympathectomy or roentgen treatment in tuberculous laryngitis are identical. Both treatments control mechanically painful dysphagia and produce reflex intralaryngeal vasodilatation. The results reported in the literature concerning the effects of both treatments on infiltration or ulceration of the laryngeal mucosa are conflicting. He prefers the roentgen treatment, since it can be administered in all cases, regardless of the local condition of the disease and of the general condition of the patient. If it is given in the precise dose and with the proper technique, accidents and complications do not follow. Furthermore, it is advisable to avoid, whenever possible, bleeding and prolonged or complicated operations in tuberculous patients. The roentgen treatment can be given as an ambulatory treatment and repeated at certain intervals. He believes

that the benefits of repeated roentgen therapy are more lasting than those obtained from sympathectomy.

Safranek[151] describes x-ray treatment in patients with tuberculous laryngitis, and gives the dosage. He has treated 300 cases in all, and in infiltrative or "productive" cases obtained a cure in 70 per cent. X-rays were not used in advanced cases of the exudative type, but they have been found helpful in relieving dysphagia. He concludes that x-rays have proved to be of great service in the treatment of laryngeal tuberculosis.

Eschweiler[152] finds carbon-dioxide snow useful in early types of tuberculosis of mucous membranes.

The surgical treatment of carcinoma of the larynx continues to make progress, and may now be regarded as the most satisfactory method of treatment. Looper[153] states that in a series of thirty-five cases no serious operative complications or fatalities have occurred. The convalescence has been satisfactorily rapid and pleasing. These patients are not depressed, and most of them are made happy and given a new lease on life with the aid of the artificial larynx.

REFERENCES

1. Larsell, O., and Fenton, R. A.: Sympathetic Innervation of the Nose; Research Report. Arch. Otolaryng., 24:687 (Dec.), 1936.

2. Higbee, D. R.: The Autonomic Nervous System: Some Fundamentals for Otolaryngologists. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:385 (June), 1936.

3. Kuntz, A.: The Autonomic Nervous System in Relation to Otolaryngology. J. A. M. A., 107:334 (Aug. 1), 1936.

4. Kuntz, A.: Pathways Involved in Pains of Nasal and Paranasal Origin Referred to the Lower Cervical and Upper Thoracic Segments and the Upper Extremity. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:394 (June), 1936.

5. St. Ernyei: Die Elemente der Nasennerven. Arch. Ohr., u. s. w. Heilk., 142:97 (Nov. 21), 1936.

6. Lyman, H. W.: Some Sphenopalatine Syndromes: Review of Sluder's Observations on the Sphenopalatine Ganglion. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:362 (June), 1936.

7. Hoover, W. B., and Poppen, J. L.: Glossopharyngeal Neuralgia. J. A. M. A., 107:1015 (Sept. 26), 1936.

8. Neivert, H., and Bilchick, E. B.: Primary Hemangioma of the Nasal Bone. Arch. Otolaryng., 24:495 (Oct.), 1936.

9. Biegeleisen, H. I.: Telangiectasia of the Nose: Treatment of Micro-injection of Sclerosive Fluid. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45: 416 (June), 1936.

10. Benjamins, C. E.: Angeborene Epithelgänge und Cysten auf dem Nasenrücken. Acta Oto-Laryng., 24:284, 1936.

11. Weinhold, H.: Impfinfekte an der Nase nach Kuhpockenimpfung. Arch. Ohr., u. s. w. Heilk., 142:208 (Dec.), 1936.

12. Buhrmester, C. C.: Nasal Mucin. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:687 (Sept.), 1936.

13. Buhrmester, C. C., and Wenner, W. F.: Presence of a Histamine-like Substance in Nasal Mucosa, Nasal Polypi and Nasal Secretion. Arch. Otolaryng., 24: 570 (Nov.), 1936.

14. Chavanne, L.: Sécrétion Nasale et Glande Thyroïde. Oto-Rhino-Laryng. Internat., 20:653 (Oct.), 1936.

15. Zaritzky, L. A.: Über Altersveränderungen der Schleimdrüsen und des Atmungsgebietes des Nase. Monatschr. f. Ohrenh., 70:1057 (Sept.), 1936.

16. Schuster, S. A.: A Method of Study of the Nasal Mucosa in Relation to the Tubercle Bacillus. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 46: 124 (Mar.), 1937.

17. Snyder, J., and Feldman, M.: Rhinoliths: Report of Three Cases with a Review of the Literature. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:430 (June), 1936.

18. Goodman, M.: Nasopalatine Duct Cysts. Radiology, 26:151 (Feb.), 1936.

19. Weidlein, I. F.: Mixed Tumor of the Nasal Septum: Report of a Case. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:574 (June), 1936.

20. Weidlein, I. F.: Hemangioma of the Nasal Septum: Report of Three Cases. Arch. Otolaryng., 23:682 (June), 1936.

21. Richter, H.: Zur Frage der Ursache der Angeborenen Deformitäten der Nasenscheidewand. Hals-, Nasen- u. Ohrenarzt (Teil 1), 27:53 (Mar.), 1936.

22. Laszlo, A. F.: Practical Points on Submucous Septum Resection: Pitfalls and Corrections. Laryngoscope, 46:840 (Nov.), 1936.

23. Ombrédanne, M., and Causse, J.: Déviations Traumatiques de la Cloison Chez l'Enfant; Leur Correction Chirurgicale. Ann. d'Otolaryng., 11:1177 (Nov.), 1936.

24. Sternstein, H. J.: Nasal Obstruction in the Adult: A Quantitative Study. Arch. Otolaryng., 25:442 (Apr.), 1937.

25. Moncrieff, A.: Nasal Obstruction in the New-born. Brit. M. J., 1:1295 (June 27), 1936.

26. van Gilse, P. H. G.: Vorführung eines Kinofilms, die Atmung bei einem Neonatus mit doppelseitiger Cyoanalatresie. Acta Oto-Laryng., 24:205, 1936.

27. Kearney, H. L.: Congenital Bony Atresia of the Right Posterior Naris. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:583 (June), 1936.

28. Goodyear, H. M.: The Etiology and Treatment of Hemorrhage of the Nose and Throat; Practical Considerations in Relation to Otolaryngology. J. A. M. A., 107:337 (Aug. 1), 1936.

29. Goodyear, H. M.: Nasal Hemorrhage: Ligation of the Anterior Ethmoid Artery: Case Report. Laryngoscope, 47:97 (Feb.), 1937.

30. Heinberg, C. J.: Treatment of Hemorrhage in Nonhemophilic Patients with an Estrogenic Substance. Arch. Otolaryng., 24:758 (Dec.), 1936.

31. Goldman, J. L.: Moccasin Snake (Ancistrodon Piscivorus) Venom Therapy for Recurrent Epistaxis. Arch. Otolaryng., 24:59 (July), 1936.

32. Scal, J. C.: Report of a Case of Severe Nasal Hemorrhage Controlled by Redium Application. Laryngoscope, 46:473 (June), 1936.

33. Dochez, A. R., Mills, K. C., and Kneeland, Y., Jr.: Studies on the Common Cold; Cultivation of Virus in Tissue Medium. J. Exper. Med., 63:559 (Apr.), 1936.

34. Whalen, E. J.: Pathogenic Fungi. Arch Otolaryng., 24:436 (Oct.), 1936.

35. Montgomery, R. R.: Relationship of Climate to Diseases of the Upper Respiratory Tract. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:704 (Sept.), 1936.

36. Sewall, E. C.: Chronic Sinusitis: the Endemic Focus and Carrier of the Common Cold. Arch. Otolaryng., 24:413 (Oct.), 1936.

37. Rawlins, A. G.: Use of Sulphur Dioxide in Treatment of the Epidemic Cold. Arch. Otolaryng., 25:119 (Feb.), 1937.

38. Rake, G.: Rapid Invasion of body through Olfactory Mucosa. J. Exper. Med., 65:303 (Feb.), 1937.

39. Armstrong, C., and Harrison, W. T.: Prevention of Experimental Intranasal Infection With Certain Neurotropic Viruses by Means of Chemicals Instilled into the Nostrils. Pub. Health Rep., 51:203 (Feb. 28), 1936.

40. Richter, H.: Grundsätzliches über die Entwicklung der Nasennebenhöhlen. Arch. f. Ohren-, Nasen-u. Kehlkopfh., 141:54, 1936.

41. Richards, L.: A Study in Transillumination. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:307 (June), 1936.

42. Kettel, K.: Über Röntgenuntersuchungen von Kiefer-höhlen nach der Füllung mit Kontrastflüssigkeit. Acta oto-laryng., 23:353, 1936.

43. Marks, H. B.: Chronic Sinusitis in Children. New Eng. J. Med., 216:604 (Apr. 8), 1937.

44. Larsell, O.: Lymphatic Pathways From the Nose; Research Report. Arch. Otolaryng., 24:696 (Dec.), 1936.

45. Sohval, A. R., and Som, M. L.: Masked Sinusitis as a Cause of Obscure Fever. Arch. Otolaryng., 25:37 (Jan.), 1937.

46. Goldman, J. L.: Complications of Acute Sinusitis with Special Reference to Bacteremias. Laryngoscope, 46:500 (July), 1936.

47. Kramer, R., and Som, M. L.: Sphenoiditis with Meningitic Symptoms. Laryngoscope, 46:507 (July), 1936.

48. Wattles, M.: A Case of Benign Giant Cell Tumor of the Ethmoid Labyrinth with a Review of the Literature. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 46:212 (Mar.), 1937.

49. Arons, I.: Ossifying Fibroma of the Maxillary Sinus: Report of a Case Successfully Treated with Irradiation. Am. J. Cancer, 29:551 (Mar.), 1937.

50. Mithoefer, W.: The Treatment, Other Than Operative, of the Nasal Accessory Sinuses. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:420 (June), 1936.

51. Fitzhugh, W. M., Jr.: Neosynephrin Hydrochloride in Otolaryngology. Arch. Otolaryng., 24:425 (Oct.), 1936.

52. Woodward, F. D.: The Staphylococcus in Relation to Sinusitis, Bronchitis and Bronchiectasis. Arch. Otolaryng., 24:753 (Dec.), 1936.

53. Bryant, F. L.: Elliott Treatment of Sinus Disease. Laryngoscope, 46:853 (Nov.), 1936.

54. Van Alyea, O. E.: The Ostium Maxillare: Anatomic Study of Its Surgical Accessibility. Arch. Otolaryng., 24:553 (Nov.), 1936.

55. Shea, J. J.: Fifteen Years' Experience with Drainage Tubes after Antrostomy in Children. Arch. Otolaryng., 24:14 (July), 1936.

56. Miller, A.: The Drainage of the Maxillary Sinus; New Technique. Brit. M. J., 1:1299 (June 27), 1936.

57. Brownell, D. H.: Postoperative Regeneration of the Mucous Membrane of the Paranasal Sinuses: a Summary of the Published Investigations. Arch. Otolaryng., 24:582 (Nov.), 1936.

58. Howarth, W.: Some Points in the Technique of the Fronto-Ethmoidal Operation. J. Laryng. and Otol., 51:387 (June), 1936.

59. Yates, A. L.: Invisible Scars in External and Ethmoidal Operations. J. Laryng. and Otol., 51:715 (Nov.), 1936.

60. Sanson, R. D.: Consideracoes Sobre o Tratamento Cirurgico da Sinusite Frontal e Suas Complicacoes. Rev. Otolar. de S. Paulo., 4:279 (July-Aug.), 1936.

61. Reeves, E.: External Radical Frontal Sinus Operation with Retention of the Original Osteum Frontale. Laryngoscope, 46:446 (June), 1936.

62. Hajek, M.: Meine Erfahrungen über die Radikale Behandlung der Stirnhöhleneiterungen. Monatschr. f. Ohrenh., 70:641 (June), 1936.

63. Mosher, H. P.: Osteomyelitis of the Frontal Bone: Notes on Three Cases. J. A. M. A., 107:942 (Sept. 19), 1936.

64. Fincher, E. F., Jr.: Osteomyelitis of Skull. South. Surg., 6:53 (Feb.), 1937.

65. Jones, A. C.: Osteomyelitis of the Frontal Bone. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:726 (Sept.), 1936.

66. Williams, H. L., and Heilman, F. R.: Spreading Osteomyelitis of the Frontal Bone Secondary to Disease of the Frontal Sinus, with a Preliminary Report as to Bacteriology and Specific Treatment. Arch. Otolaryng., 25:196 (Feb.), 1937.

67. Behrens, H. C.: Osteomyelitis of the Skull of Otitic and Paranasal Sinus Origin. Arch. Otolaryng., 25:272 (Mar.), 1937.

68. Adson, A. W., and Hempstead, E.: Osteomyelitis of Frontal Bone Resulting from Extension of Suppuration of Frontal Sinus: Surgical Treatment. Arch. Otolaryng., 25:363 (Apr.), 1937.

69. Lemon, A. N.: Report of Case of Maxillary Sinusitis with Complicating, Spreading Osteomyelitis, Brain Abscess and Death. Laryngoscope, 46:754 (Oct.), 1936.

70. Coke, F.: The Treatment of Paroxysmal Sneezing. J. Laryng. and Otol., 51:522 (Aug.), 1936.

71. Clarek, J. A., Jr., and Rogers, H. L.: A Statistical Study of Allergic (Vasomotor) Rhinitis. Arch. Otolaryng., 25:124 (Feb.), 1937.

72. Linton, L. D.: A Comparison of Intradermal and Intramucosal Tests in Cases of Allergic Rhinitis. Arch. Otolaryng., 23:679 (June), 1936.

73. Benjamins, C. E.: Recherches sur la Substance Active du Pollen des Graminées. Acta Oto-Laryng., 24:153, 1936.

74. Feinberg, S. M.: Seasonal Hay Fever and Asthma Due to Molds. J. A. M. A., 107:1861 (Dec. 5), 1936.

75. Harkness, G. F.: Why I Have Not Used Iontophoresis. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 46:169 (Mar.), 1937.

76. Dean, L. W.: The Fundamentals of Allergic Rhinitis with Particular Reference to Ionization (Iontophoresis). ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:326 (June), 1936.

77. Jarvis, D. C.: Clinical Experience of a Correspondence Study Group with Suprarenal Concentrate in Otolaryngology. Laryngoscope, 47:263 (Apr.), 1937.

78. Scott-Brown, W. G.: Treatment of Recurrent Nasal Polypi with Radium. Lancet, 2:619, 1936.

79. Kurata, K.: Studien über die Ozaena. Monatschr. f. Ohrenh., 70:1075 (Sept.), 1936.

80. Reichardt, H.: Zur Frage der Heredität der Ozaena. Monatschr. f. Ohrenh., 70:389 (Apr.), 1936.

81. Amersbach, K.: 20 Jahre Ozaenabeobachtung und Behandlung. Arch. Ohr-, u. s. w. Heilk., 142:106 (Nov. 21), 1936.

82. Zakrzewski, A., and Wiza, J.: The Treatment of Ozaena by Bacteriophages. Polski Przeglad Otolaryngologiczny, 12:1 (Jan.), 1937.

83. Mörch, P.: Nachuntersuchungen von Ozänapatienten nach Manganbehandlung. Acta Oto-Laryng., 23:380, 1936.

84. Stovin, J. S.: Use of the Galvanic Current in the Treatment of Atrophic Rhinitis and Ozena: Further Observations. Arch. Otolaryng., 25:305 (Mar.), 1937.

85. Blankenhorn, M. A., and Spies, T. D.: Oral Complications of Chronic Alcoholism; Significance, Recognition, and Treatment. J. A. M. A., 107:641 (Aug. 29), 1936.

86. Hollander, L.: Treatment of Carcinoma of the Lip. Arch. Phys. Therapy, 17:17 (Jan.), 1936.

87. Campbell, J. L.: Early Diagnosis of Cancer of the Mouth. J. M. A. Georgia, 25:252 (July), 1936.

88. Ward, C. B., and Betts, A.: Epithelioma of the Lip. Radiology, 26:349 (Mar.), 1936.

89. Hare, H. F., Poppen, J. L., and Hoover, W. B.: Cancer of the Mouth: Care of the Patient Utilizing Prolonged Anesthesia Obtained by Alcohol Injection of Branches of the Fifth Nerve. New Eng. J. Med., 214:572 (Mar. 19), 1936.

90. Rosedale, S.: Intralingual Thyroid: Discussion with Report of a Large Struma Presenting in the Anterior Part of the Tongue. Annals of Otology, Rhinology and Laryngology, 45:1009 (Dec.), 1936.

91. Buckman, L. T.: Lingual Thyroid. Laryngoscope, 46:765 (Oct.), 1936.

92. Beeson, H. B.: Aberrant Goiter: with Report of an Instance of Intralaryngeal Thyroid Tumor. Arch. Otolaryng., 25:449 (Apr.), 1937.

93. Smith, F.: Lipoma of the Tongue. J. A. M. A., 108:522 (Feb. 13), 1937.

94. Spencer, F. R.: Carcinoma of the Tongue: a Review of Fourteen Cases. Arch. Otolaryng., 24:1 (July), 1936.

95. Sharp, H. S.: A Case of Absence of Salivary Secretion. J. Laryng. and Otol., 52:177 (Mar.), 1937.

96. Aboulker, P.: Un cas de Maladie de Mikulicz. Ann. d'Oto-Laryng., p. 893 (Sept.), 1936.

97. Ruppe, C., Lattès and Voisin (Mme.): A Propos de Cinq Observations de Lithiase Parotidienne. Ann. d'Oto-Laryng., p. 577 (June), 1936.

98. Csillag, A.: Der praktische Wert der Sialoadenographie in der Diagnostik der Intermittierenden Speicheldrüsenschwellungen. Acta Oto-Laryng., 23:481, 1936.

99. Kunstmann, H.: Über Parotisadenome und ihre Pathogenese. Frankfurt. Ztschr. f. Path., 49:214, 1936.

100. Harris, P. N.: Adenoma of the Salivary Glands. Am. J. Cancer, 27:690 (Aug.), 1936.

101. Olson, G. W.: Pulmonary Metastases Occurring from Aberrant Mixed Salivary Gland Tumors. Report of Three Cases and Discussion. Laryngoscope, 47:252 (Apr.), 1937.

102. Minear, W. L., Arey, L. B., and Milton, J. T.: Prenatal and Postnatal Development and Form of Crypts of Human Palatine Tonsil. Arch. Otolaryng., 25:487 (May), 1937.

103. Meeker, L. H.: Histopathological Studies; the Mucous Glands Related to the Tonsil; the Relation of the Tonsil to Bronchiogenetic Cysts. Laryngoscope, 47:164 (Mar.), 1937.

104. Urbantschitsch, E.: Histologische Reihenuntersuchungen von Tonsillen und Adenoiden Vegetationen. Monatschr. f. Ohrenh., 70:1177 (Oct.), 1936.

105. Menzel, K. M.: Ueber Tuberkelbazillenbefunde in den Gaumenmandeln. Monatschr. f. Ohrenh., 71:83 (Jan.), 1937.

106. Smith, H. D.: Follow-up of Patients Eight Months after Tonsillectomy. Arch. Otolaryng., 24:488 (Oct.), 1936.

107. Barwell, H.: The Nose and Throat in Relation to Rheumatic Diseases. Lancet, 1:67 (Jan. 9), 1937.

108. Waldbott, G. L., Ascher, M. S., and Giese, F. W.: Results of Tonsillectomy in Allergic Patients; Follow-up Study of 433 Cases. J. Michigan M. Soc., 35:369 (June), 1936.

109. Jackson, H., Jr., Parker, F., Jr., and Brues, A. M.: Malignant Lymphoma of the Tonsil. Am. J. M. Sc., 191:1 (Jan.), 1936.

110. Neffson, A. H., and Brem, J.: Diphtheria Simulating Peritonsillar Abscess: Dangers of Incision. Arch. Otolaryng., 25:260 (Mar.), 1937.

111. Linck, A.: Für die grundsätzliche Abscesstonsillektomie. Arch. f. Ohren,- Nasen- u. Kehlkopfh., 141:255, 1936.

112. Linck, A.: Die Verhütung der Tonsillogenen Sepsis durch Abscess-Tonsillektomie. Ztschr. f Hals-, Nasen- u. Ohrenh., 39:329, 1936.

113. Schroeder, R.: Some Remarks on Surgical Treatment of Peritonsillar Inflammations. J. Laryng. and Otol., 51:574 (Sept.), 1936.

114. Thacker, Neville, W. S.: Radical Treatment of Peritonsillar Abscess. J. Laryng. and Otol., 51:650 (Oct.), 1936.

115. Merica, F. W.: Tonsillectomy as a Cure for Peritonsillar Abscess, with Case Reports. Arch. Otolaryng., 25:521 (May), 1937.

116. Boemer, L. C.: The Great Vessels in Deep Infection of the Neck. Arch. Otolaryng., 25:465 (Apr.), 1937.

117. Schroeder, R.: Some Remarks on Suppuration in the Para-pharyngeal Space. J. Laryng. and Otol., 51:631 (Oct.), 1936.

118. Tavani, E.: Tromboflebite del Seno Cavernoso di Origine Tonsillare. Boll. d. Mal. d. Orecchio, d. Gola, d. Naso, 54:378 (Oct.), 1936.

119. Jauerneck, A.: Geheilte Isolierte Kauernosusthrombose Wahrscheinlich Tonsillogenen Ursprungs. Hals-, Nasen- u. Ohrenarzt (Teil 1), 27:271, 1936.

120. Grove, W. E.: Septic and Aseptic Types of Thrombosis of the Cavernous Sinus; Report of Cases. Arch. Otolaryng., 24:29 (July), 1936.

121. Lillie, H. I.: The Clinical Significance of Compensatory Granular Pharyngitis. Arch. Otolaryng., 24:319 (Sept.), 1936.

122. Schenck, H. P.: Chronic Infections in the Pharynx: a Pathologic Study. Arch. Otolaryng., 24:299 (Sept.), 1936.

123. Brown, L. E.: The Pharyngeal Lymphatics as a Focus of Infection. Annals of Otology, Rhinology and Laryngology, 45:447 (June), 1936.

124. Stout, P. S.: Dry-ice (Carbon Dioxide Ice) Burn of Throat. Laryngoscope, 46:992 (Dec.), 1936.

125. Richards, L.: Retropharyngeal Abscess. New Eng. J. Med., 215:1120 (Dec. 10), 1936.

126. Schall, L. A.: Aberrant Vessel of the Posterior Pharyngeal Wall. Annals of Otology, Rhinology and Laryngology, 45:891 (Sept.), 1936.

127. Pilcher, R.: Diagnosis of Malignant Disease of the Pharynx. Brit. M. J., 1:13 (Jan. 2), 1937.

128. Albright, H. L.: Management of Fibroma of the Retropharynx; Report of Case. New Eng. J. Med., 214:242 (Feb. 6), 1936.

129. Torres, C. M., and Monteiro, A.: Neurinoma Retropharyngeo Contendo Cystos em Communicaçao com a circulaçao Arterial. Mem. Inst. Oswaldo Cruz, 31:873 (Dec.), 1936.

130. Kanas, S.: Ein Fall von "Malignem Granulom" des Rachens. Acta Oto-Laryng., 23:429, 1936.

131. Howarth, W.: Some Tumors and Ulcers of the Palate and Fauces; Semon Lecture, 1936. J. Laryng. and Otol., 52:1 (Jan.), 1937.

132. Hill, F. T.: Malignant Disease of the Sinuses and Nasopharynx, in the Small Hospitals. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 46:158 (Mar.), 1937.

133. Flynn, R.: Case of Naso-Pharyngeal Fibroma. Australian and New Zealand J. Surg., 6:179 (Oct.), 1936.

134. Blumenfeld, L.: Plasma Cell Tumors of the Nose and Nasopharynx. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:436 (June), 1936.

135. Lemaitre, F., Ardoin, G., and Lemaitre, Y.: Introduction á l'Étude des Tumeurs dites "Cylindromes." Acta Oto-Laryng., 24:112, 1936.

136. Goldsmith, P. G., and Ireland, P. E.: Mixed Tumors in the Nose and Throat. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:940 (Dec.), 1936.

137. Tucker, G.: Laryngoptosis: Ptosis of the Larynx Due to Downward Displacement of the Hyoid Bone Resulting from Fibrosis and Shortening (Congenital Anomaly) of the Left Sternohyoid and Sterno-Thyroid Muscles. Arch. Otolaryng., 25:389 (Apr.), 1937.

138. Furstenberg, A. C.: An Anatomical and Clinical Study of Central Lesions Producing Paralysis of the Larynx. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 46:39 (Mar.), 1937.

139. Lore, J. M.: A Suggested Operative Procedure for the Relief of Stenosis in Double Abductor Paralysis: an Anatomic Study. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45-679 (Sept.), 1936.

140. Sercer, A.: Zur Operativen Therapie Chronischer Kehlkopfstenosen. Monatschr. f. Ohrenh., 10:1153 (Oct.), 1936.

141. Hofer, G., and Motloch, T.: Membranöse Verwachsungen der Stimmbänder. Monatschr. f. Ohrenh., 70:576 (May), 1936.

142. Tucker, G.: Inflammatory Tumors of the True Vocal Cords, Direct Laryngoscopic Observations. J. Laryng. and Otol., 51:563 (Sept.), 1936.

143. Koch, J.: Die Bedeutung der Bestrahlungstechnik und des Gewebsaufbaus für den Erfolg der Röntgenbestrahlung von Larynxpapillomen. Arch. f. Ohren-, Nasen- u. Kehlkopfh., 142:83, 1936.

144. Palmer, A., and Mehler, L.: Recurrent Lipoma-Myxochondroma-Fibroma of the Larynx; a Case Exhibiting Unique Features. Laryngoscope, 46:653 (Sept.), 1936.

145. Cummings, G. O.: Lymphosarcoma of the Larynx: Report of a Case. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:578 (June), 1936.

146. Clerf, L. H., and Bucher, C. J.: Blastomycosis of the Larynx. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:923 (Dec.), 1936.

147. Schuster, F. P.: Observations of the Larynx in the Tuberculous. Arch. Otolaryng., 25:23 (Jan.), 1937.

148. Blegvad, N. R.: The Problem of Early Laryngeal Tuberculosis. J. Laryng. and Otol., 52:153 (Mar.), 1937.

149. Hautant, A.: Abnormal Forms of Tuberculosis Simulating Cancer of the Larynx and Their Converse. J. Laryng. and Otol., 52:65 (Feb.), 1937.

150. Rubaltelli, E.: Simpaticectomie Periarteriose e Röntgenirradiazioni Nella Cura Della Laringite Tubercolare. Oto-Rhino.-Laring. Ital., 6:558 (Dec.), 1936.

151. Safranek, J.: Actualités Dans la Pathologie et le Traitement de la Tuberculose Laryngie. Acta Oto-Laryng., 23:242, 1936.

152. Eschweiler, H.: Die Vereisungsbehandlung der Schleimhauttuberkulose. Ztschr. f. Hals-, Nasen- u. Ohrenh., 41:129, 1936.

153. Looper, E. A.: Laryngectomy for Cancer of the Larynx. Surg., Gynec. and Obst., 64:524 (Feb.), 1937.

154. Gruenfeld, G. E., and Jorstad, L. H.: Adenoma of the Parotid Salivary Gland: Onkocyte Tumor. Am. J. Cancer, 26:571 (Mar.), 1936.

LXXXII

TONSILLECTOMY FOR RHEUMATISM: A STUDY OF 3,172 CASES

WM. H. TURNLEY, M.D.

STAMFORD, CONN.

Rheumatism is one of the great medical problems of civilization, especially in the temperate zone. Since the etiology of this disease is still obscure, there is no uniformity in the usage of the word "rheumatism" as applied without discrimination to all kinds of arthritis, and also to conditions which have nothing to do with the joints. In this study, painful conditions of the muscles, fascia, bones, nerves and joints are all alike termed rheumatism.

For the most modern classification of rheumatism, preference is given to the one unanimously adopted by the directors of arthritic clinics in New York, which divides rheumatism into six main headings:

I. Infectious
   1. Rheumatic fever
   2. Rheumatoid arthritis
   3. Arthritis caused by specific organism

II. Degenerative
   1. Osteo-arthritis (hypertrophic arthritis)

III. Allergic
   1. Serum sickness

IV. Traumatic

V. Metabolic
   1. Gout
   2. Scurvy
   3. Rickets

VI. Neurogenic arthropathy. Including syringomyelitic, Charcot's, posthemiplegic, etc.

It is of particular importance to note that rheumatoid arthritis is included in the infectious group, since it is now generally accepted as a disease of bacterial origin. A large group of patients suffering from this type of rheumatism is included in this study.

Patients referred to here are all ambulatory cases which have been observed in the Tonsil Clinic of the Manhattan Eye, Ear and Throat Hospital in New York City during a period of six years, beginning in November, 1930. For convenience the following table shows the number of such patients operated upon, with the percentage of those giving a rheumatic history:

	1931	1932	1933	1934	1935	1936	Total
Number of patients examined	14,321	14,301	12,779	12,994	12,770	10,584	77,749
Number of tonsil operations	11,925	12,001	10,583	10,698	10,212	9,834	65,253
Pts. returned for postop. exam.	10,075	10,151	8,834	9,522	8,937	9,464	56,983
Pts. with rheumatic history	721	776	694	636	1,010	982	4,819
Rheumatic pts. operated upon	613	668	586	528	592	559	3,546
Postop. rheumatic pts. exam.	553	604	516	469	518	512	3,172
Percent pts. with rheum. hist.							7%

Incidentally, out of a total of 65,253 operations, there were six deaths, not one of which was due to hemorrhage directly. One patient was a hemophiliac, but died of pneumonia; one died of heat prostration; one of septicemia; one from ether narcosis; one from acute edema of the thymus; and one was reported as status lymphaticus. In other words, there was one death in eleven thousand operations.

The method of obtaining this information was to have the tonsil clinic a separate unit of the nose and throat service, in charge of one surgeon. A separate card is kept for each tonsil patient with a space for his or her rheumatic history. A week after operation, patients return to the clinic for a postoperative inspection. Three months later they are requested to return for a second inspection. At the end of one, two, three, four, five and six years the rheumatic patients are selected, and a card is sent asking them to come again for inspection; or a return form card is sent with the following questions to be answered:

1. Since your tonsils have been removed has your rheumatic condition been improved, no change, or worse?
2. Has your general health been improved or not?
3. Have you noticed any bad effects in any way since your tonsils were removed? If so, what?

For detailed procedure, reference is made to Dr. David Jones' paper given in the symposium on tonsils at the 1934 meeting of the American Academy of Medicine at Chicago.

About seven per cent of the patients examined gave a history of some form of rheumatism. About twenty-five per cent of the

rheumatic patients gave a history of some heart condition. A goodly number gave a history of impaired hearing, which may be due to a rheumatic condition of the ossicles of the ear; but the percentage was not recorded. About six per cent of the rheumatic patients, mostly under twenty years of age, gave a history of acute rheumatic fever; but no attempt was made to segregate this group, it being included with the others of the great rheumatoid arthritic group. It is interesting to note, however, that several patients reported having suffered from rheumatic fever since their tonsils were removed.

There is a definite group of patients with symptoms of pain radiating from the sphenopalatine ganglion, which may be termed a syndrome, and has been thoroughly described by Sluder. Aches and pains which patients attribute to a neuralgic condition in the shoulder and neck, originate behind the auricle; they radiate towards the trapezius muscle of the shoulder, neck and occiput, and down the deltoid muscle of the arm. Such pains are commonly unilateral at first rather than bilateral. Mastication may be painful on account of an associated involvement of the bony portion of the external canal, which is in close proximity to the glenoid fossa. The sterno-cleidomastoid and other muscles of the neck attached to the mastoid, account for pain when the head is moved. Torticollis may be present, due to fixation of the muscles to avoid pain upon movement. This condition, described by the patient as a crick in his neck following a sore throat and cold, may be termed myo-synovitis.

There seems to have been indications of Sluder's syndrome at some period of the patient's life before he realized his rheumatic condition. Thus, we can date the onset of his rheumatism from these pains which are aggravated by damp or cold weather and a low barometric pressure. If a careful history is obtained, a great many patients will recall an associated sore throat; which in ninety per cent of the cases is nothing but a form of tonsillitis. Rheumatic patients with a focus of infection other than the tonsils do not seem to complain of this syndrome, unless the maxillary antrum is involved. In other words, this myo-synovitis of the shoulder may be a premonitory symptom of a tonsillar rheumatism.

As shown in the table, during the past six years 65,253 patients were operated upon. There were 4,819, or about seven per cent, with a history of rheumatism, of which 3,546 were operated upon, but only 3,172 returned for a postoperative examination. (A recent survey of the State of Massachusetts shows about three per cent of the total population suffering from rheumatic disease; which exceeds the number afflicted with cancer, tuberculosis and heart disease com-

bined.) At the end of six years, about seventeen per cent of those to whom cards were sent had returned to the clinic or mailed answers to our questions. In consequence, this series does not represent a complete record of patients operated upon. It does represent 3,172 patients who, after a postoperative examination, made report in person or by card at least once during the six-year period.

Of these patients, sixty-six per cent were women and thirty-four per cent men. A larger proportion of the men had rheumatism, but more women returned for a checkup, either because women can arrange their time more conveniently, or else are more conscientious. Among the patients thirty-three per cent were Hebrews, four per cent Colored, and no Chinese. (It happened that the Chinese patients operated upon did not have rheumatism; but on questioning a number of them it was found that they have rheumatism in China as well as in the United States under similar conditions.) The remaining sixty-three per cent included many nationalities, of which a very noticeable proportion was Puerto Rican. Upon questioning these patients as to why they wanted their tonsils removed, the general opinion was that they have very little rheumatism in Puerto Rico, but after residing in this climate they develop sore throats, followed by pains in various parts of the body, which seem to be relieved to some extent by having their tonsils removed.

There is, in any infection of the tonsils, a definite relation to many pathological conditions, which varies with different climatic areas and different races. In tropical and subtropical countries the tonsils of children seldom become infected, and are rarely suspected where certain diseased conditions are noted; in colder regions tonsillitis is more prevalent among children. The same observation holds true of rheumatism among adults, and this observation may not be merely incidental.

The history of these patients consists of aches and pains in various parts of the body and at various times, intermittently, from three weeks to twenty-five years. Some have single attacks and some have repeated attacks. Colored patients describe this condition more vividly than any textbook by saying: "Doctor, I'se just got misery in all my bones." Some patients report an associated sore throat; while a great many report *no tonsil trouble whatever*, except for a feeling of fullness in the throat and a constant desire to expectorate. It is difficult to convince such patients that tonsillectomy may better their condition.

It has been observed, also, that the rheumatic type of tonsil is not the large follicular tonsil with pus (staphylococci), but rather

the small obscure tonsil, which on pressure exudes from its crypts a thin secretion that trickles down the back of the oro-pharynx causing part of that postnasal drip and cough. This is usually some type of streptococci infection, or mixed infection with streptococci. In other words, the size of the tonsil has nothing to do with the potency of the toxin liberated by the organisms present; a small rattlesnake is more venomous than a large boa constrictor. The bacteriology of these rheumatic tonsils will not be discussed in this paper, but a consensus of opinion seems to incriminate a streptococcus of some strain, usually the hemolyticus.

On closer inspection, this rheumatic type of tonsil shows a purplish red color of the anterior pillar, particularly the portion overlying the upper half and on to the edge of the soft palate, but very seldom on the uvula. This differs from the well-known "smoker's throat," which shows obvious pharyngeal rather than tonsillar irritation, and is more of a salmon-colored stippling. This is the type of infection in which a sore throat is rarely mentioned; it may be so free of objective manifestations that the patient is not conscious of any disease; yet there is a constant absorption from such foci, though the toxic or bacterial activity may be mild or of a low grade type. It is the insidiousness of such tonsils that makes them so pernicious; they are wolves in sheeps' clothing. This juicy, red, chronic tonsil may be termed the "rheumatic type"; at times it may flare up or become superimposed with an extraneous type of organism, invoking an acute condition.

It is no longer controversial that a very small tonsillar remain (sometimes so small as to be visable only during an acute flare-up) may be more lethal than the entire gland. These fragments, even when not acutely active, may give rise to a chain of toxic symptoms, often attributed to other causes. Tonsil removal should be done by a specialist in a surgical manner, rather than by electrocoagulation or some other method, and the slogan should be, "All or None."

The ages of patients operated upon varied from three to sixty-nine years. The duration of attacks also varied, intermittently, from a few months to twenty years. That is, some had attacks when young, and not another attack until years later. Others had attacks of shorter duration, but at more frequent intervals. By far the greatest percentage of rheumatism was in the group from thirty to forty years of age. The younger cases were described by their mothers as having growing pains, or acute rheumatic fever. The older cases included some with osteo-arthritis, as shown in the table below:

Ages		Per cent
3 to 10	Mostly indefinite pains and	7
10 to 20	and acute rheumatic fever	10
20 to 30	Mostly rheumatoid arthritis and myosynovitis	15
30 to 40	Mostly rheumatoid arthritis	37
40 to 50	Mostly rheumatoid arthritis	23
50 to 60	Mostly rheumatoid arthritis	7
60 to 70	Mostly rheumatoid arthritis and osteo-arthritis	1

In reviewing this table it is well to remember that these are all ambulatory cases, and though some over sixty years of age came in with an osteo-arthritis it was not deemed advisable to remove their tonsils for this condition alone. Then, too, many of these tonsillectomies were performed as a prophylactic measure against rheumatism.

As to results, it was difficult to figure for each age the percentage cured, better, unimproved, or worse. The average was about eighty-three per cent giving a history of either no further trouble or definitely better. About twelve per cent said they had noticed no difference, and about five per cent said they were worse. There were some who were relieved immediately, but the big majority showed improvement within the year. Curiously enough, some reported their rheumatism worse, or they had an acute attack immediately following the operation. This may be considered a good omen, showing that the operation hit the focus of infection, causing a flare-up which later improved. The younger the patients and the shorter the duration of the rheumatism, the more marked the improvement, and vice versa. Of those that gave a history of no improvement, almost all had some complication or other foci of infection, such as a sinus involvement or carious teeth. Also, they were past their youth, and one could not expect too encouraging results from patients with bony proliferation, as in the osteo-arthritic group. Of those who became worse, not one said he was worse because of operation. On the contrary, most of them were benefited in one way or another. This is an excerpt from a typical report: "Three years ago I had a tonsil operation at your hospital * * * * the operation has made a tremendous improvement in my health. I had been suffering from arthritis for seven months before the operation but it was entirely cured within three months after the operation."

H. B. Graham, of San Francisco, recently reported a series of three thousand cases from the Southern Pacific Hospital, of which four hundred and thirty-eight gave a history of rheumatism. After a tonsillectomy three hundred reported no further trouble, one hundred about the same, and thirty-eight no improvement or worse. Similar results are reported by Kaiser, Smith, Graham, Mackenty and other writers named in the bibliography.

Among other classes of rheumatism, those that are due to specific organisms need not be discussed here. Degenerative types such as osteo-arthritis, are not helped. Allergic cases, including serum sickness, present too large a subject for this paper. Those due to trauma are relieved in that the offending focus may have been removed. Metabolic types such as scurvy and rickets are rare; but gout will be found more prevalent if correctly diagnosed.

At this point it may not be too far amiss to revive that old question whether the tonsils should be removed, and when. No set rule can be laid down, each case requiring special consideration. However, there is probably little or no harm done by removing tonsils and adenoids in any person over five or six years of age, since their function has apparently come to an end by this age. Some people may argue that nature placed the tonsils there for a purpose. Perhaps; but after they have become infected they are a menace. A policeman is a good man to have in a community to protect us from the lawless; but a corrupt policeman is worse than no policeman at all, for he is in league with the criminal.

A review of the anatomy of the tonsils, calling attention to crypts and lymphatics may be helpful here. "The crypt of a tonsil is its peculiar and most characteristic structure. It consists of an invagination of the epithelium from the surface of the tonsil, which has undergone a very interesting anatomical change. The subepithelial connective tissue, which is present to a marked degree beneath the surface epithelium, disappears as soon as the epithelium begins to form crypts. This permits the epithelial cells to come in direct contact with the lymphatic structure of the tonsil. The relation of the tonsil to the lymphatic vessels is here somewhat different from other parts of the body; for the lymphatic vessels have their origin in the tonsil itself, and from here drain into the deep cervical chain of glands underneath the sternocleidomastoid muscle, thence to the thoracic glands, and finally into the thoracic duct." By this route infection is carried to all parts of the body. As early as 1784, William Hunter described the lymphatic system as the general absorptive system of the whole body.

To enumerate specific indications for a tonsillectomy, the following classification has been arranged:

I. Evidence of infection
   1. Throat
      a. Frequent attacks of sore throat (90% tonsillitis)
      b. Cheesy plugs in the crypts causing foul odor
      c. Keratosis leptothrix of the tonsil

d. Quinsy and retro-pharyngeal abscesses
e. Chronic laryngitis (non-specific)

2. Ear
   a. Otitis media in children (under two years adenoids only are removed)
   b. Tubal catarrh with otalgia

3. Eye
   a. Certain cases of involvement of uveal tract
   b. Chronic conjunctivitis
   c. Optic neuritis (certain cases)

4. Nose
   a. Stubborn sinus infections (remember that adults frequently have adenoids)
   b. A & T is a preliminary step to most sinus operations

5. General
   a. Enlarged neck glands of Waldeyer's ring with colds (evidence of infection in this area)
   b. General systemic rundown condition, especially in children, as evidenced by backwardness in school
   c. Diphtheria carriers
   d. Cardio-nephritic cases
   e. Certain thyroid cases.
   f. Rheumatism and *all* allied conditions
   g. It may be a prophylactic measure against T. B., possibly Hodgkin's disease and others

II. Mechanical obstruction
   1. Adenoids cause difficult breathing; enlarged tonsils may cause vomiting in children

III. Allergic conditions, such as asthma, are helped in some cases; hay fever and rhinorrhea are doubtful

IV. Some schools, insurance companies, industrial plants and business houses require it for the above reasons.

In conclusion, rheumatism is one of the great problems of civilization in the temperate zone. It is a lesser problem as one nears the equator, following that source of all energy, the sun. It is in some mysterious way related to focal infection; but this focal infection does not explain the entire problem. Since the tonsils are probably the greatest source of infection, because of their direct

communication with the lymphatic system, it would seem logical to advocate their removal in all rheumatic cases until the etiology of rheumatism is better known.

SUMMARY

1. Rheumatism is benefited by removing a focus of infection, chiefly the tonsil.

2. Sluder's syndrome seems to be one of the first manifestations of rheumatism through the tonsillar portal of entry.

3. The tonsil is the most frequent portal of entry for bacteria, due to its uniquely direct connection with the lymphatic system and blood stream.

4. The rheumatic type is not the enlarged acutely inflamed tonsil; it is rather the small, chronic, juicy tonsil.

5. All rheumatic patients should have their tonsils removed, if their general physical condition permits.

DISCUSSION

This paper is not intended to convey the impression that a tonsillectomy is a panacea for rheumatism. The disease calls also for medical and therapeutical measures, and there are some recent chemicals which seem hopeful. Many people have foci of infection, yet never develop rheumatism, and some have rheumatism in which a definite focus cannot be found. There still remains an unknown factor; but removal of infected tonsils is one of the essentials of modern treatment.

810 GURLEY BLDG.

BIBLIOGRAPHY

1. Cecil, Russell L.: Rheumatoid Arthritis. J. A. M. A., 100:1220 (April 22), 1933. (Other references from this work.)

2. Jones, David H., Nisson, H. A., and Kaiser, A. D.: Symposium on Tonsils. Trans. Am. Acad. Ophthal. and Otolaryng., 1934.

3. Mackenty, John E.: Upper Respiratory Focal Infections. Bull. New York Acad. Med., 8:2 (Feb.), 1931. (Other references from this work.)

4. Pavey-Smith: Tonsillectomy in Chronic Arthritis. Lancet, 1:170-173, 1929.

5. Graham, H. B.: The Treatment of Rheumatism. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 44:181 (March), 1935.

6. Kaiser, A. D.: The Relation of Tonsils to Acute Rheumatism During Childhood. Amer. J. Dis. Child., 37:559 (March), 1929.

7. Billings, Frank: Chronic Focal Infections and Their Etiologic Relations to Arthritis and Nephritis. Arch. Ont. Med., 9:484 (April), 1912.

8. Jackson and Coates: Textbook of Ear, Nose and Throat. W. B. Saunders Co., 1937.

9. Lyman, H. W.: Some Sphenopalatine Syndromes: A Review of Sluder's Observations. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 45:362 (June), 1936.

10. Lierle, D. M.: Focal Infection in Arthritis. Trans. Amer. Acad. Ophth. and Otolaryng., page 25.

11. Turnley, Wm. H.: Results From 76,000 Adenoid and Tonsil Operations. Laryngoscope, 47:1 (Jan.), 1937.

12. Batson, O. V.: Lymphatic Drainage of the Head. Trans. Amer. Acad. Ophth. and Otolaryng., p. 553, 1936.

LXXXIII

OBSERVATIONS IN THREE HUNDRED CASES OF ACUTE MASTOIDITIS

GEORGE C. KREUTZ, M.D.
AND
GORDON L. WITTER, M.D.

DETROIT

In this paper are presented the results of the study of three hundred cases of acute mastoiditis in which simple mastoidectomy was performed in the Division of Otology of the Henry Ford Hospital from 1926 to 1936. The study was undertaken to determine (1) the value of surgical incision of the tympanic membrane in comparison with allowing spontaneous rupture to occur; (2) the predisposing causes of mastoiditis; (3) the bacteriology of uncomplicated and complicated mastoid infections; (4) the optimum time to operate; (5) and to compare vigorous postoperative treatment with a modified passive procedure.

The age of our patients varied from three months to sixty-eight years. One hundred and thirty-one patients were female and one hundred and sixty-nine were male. The right mastoid was involved in one hundred and seventy cases, the left in one hundred and four, and there was bilateral infection in twenty-five. Dividing the cases into two groups, viz., "A" where surgical incision of the drum was done, and "B" where the membrane was allowed to rupture spontaneously, we studied the cases with respect to (1) duration of earache before the onset of aural discharge; (2) duration of aural discharge prior to mastoid operation; (3) duration of aural discharge after operation; and (4) total duration of postoperative care. We found that pain prior to discharge varied from one to eight days in each group, but in group "A" where paracentesis was performed, the average was 1.5 days, whereas it was 3.1 days for group "B" where rupture was spontaneous. Aural discharge lasted from two to forty-nine days for an average of 15 days in group "A" as compared with six to one hundred and twenty days for an average of 30 days in group "B". Aural discharge persisted after operation for 6.5 days in "A" and for 10 days in "B". Total postoperative care in "A" averaged 34 days; in "B" 39 days. In other words, all conditions were more favorable when the drum was

incised instead of being allowed to rupture. Paracentesis also was advantageous in that (1) it afforded earlier relief of pain and allowed rest; (2) it permitted the collection of uncontaminated cultures from the middle ear cavity; (3) it tended to lessen complications, for, as will be shown later, only eleven cases developed complications, eight recovering and three dying, contrasted with thirty-seven complications, thirteen of them fatal, when the drums were allowed to rupture.

Bacteriology.—Cultures taken from the mastoid cavities at the time of operation were reported as follows:

Streptococcus Hemolyticus	63%
Streptococcus Viridans	8%
Staphylococcus Aureus	3%
Staphylococcus Albus	6%
Pneumococcus	7%
Type 1	2 cases
Type 2	2 cases
Type 3	16 cases
Type 4	1 case
Negative Cultures	9%

Complications.—Complications occurred in forty-eight cases, or 16 per cent of the total group that was operated upon. Their character was as follows:

Persistent otorrhea	21 cases—7%
Lateral Sinus Thrombosis	12 cases—4%
Meningitis	9 cases—3%
Brain Abscess	3 cases—1%
Septicemia	3 cases—1%

Of one hundred eighty-nine cases infected with hemolytic streptococus eight died—approximately 4 per cent. Of sixteen cases infected with pneumococcus type 3, eight died—50 per cent. In other words, pneumococcus type 3 proved twelve times as deadly as the streptococcus in mastoid disease complications. This strongly emphasizes the need for culturing the middle ear at the time of paracentesis as emphasized by Page[1] in his studies of mastoid infections at the Manhattan Eye, Ear, Nose and Throat Hospital. Early observation by an otologist would likely assist in the diagnosis and treatment of the usual attending paranasal sinus and throat infection and would enhance his value in assisting in deciding upon an optimum time for surgical intervention should this be necessary. Our statistics indicate that there are fewer complications when mastoid operations are performed during the second and third weeks of the course of the mastoid infection, as previously reported by Guthrie[2] of Edinburgh.

Time of Operation:

1. Operation in 1st week	53 cases
Complications with recovery	3 cases
Complications with death	12 cases
2. Operation in 2nd week	70 cases
Complications with recovery	7 cases
Complications with death	1 case
3. Operation in 3rd week	85 cases
Complications with recovery	3 cases
Complications with death	none
4. Operations in the 4th week or later	92 cases
Complications with recovery	19 cases
Complications with death	6 cases

It would, therefore, seem unwise, as a rule, to operate during the first week when the mastoid infection is poorly localized. Likewise, complications of a serious nature seem to increase if operation is delayed beyond four weeks. The second and third weeks seem to be the optimum time at which to perform simple mastoidectomy.

Predisposing Causes.—In our series of three hundred cases, 42.5 per cent presented frank clinical evidence of paranasal sinus disease, and we feel inclined to believe that if further methods of diagnosis had been used more fully, particularly the x-ray and the nasopharyngoscope, the total would be higher; 62.5 per cent of the total number had not had tonsillectomy or adenoidectomy.

In seventeen recurrent mastoid infections, and in all twenty-one cases that developed chronic otorrhea, sinus disease was definitely present. Tonsils and adenoids had not been removed in four cases that developed chronicity and in twenty-one cases that recurred. From these figures one might infer that sinus disease, chronically infected tonsils and adenoids are predisposing factors in the primary etiology, as well as of recurrence and chronicity of middle ear and mastoid disease. This inference is in accord with the published statements of Campbell[3] who found sinus disease and acute otitis media associated in one hundred cases; and with that of Fowler[4] who reported 86 per cent of cases so associated, with special emphasis placed on the importance of sinus disease as a cause of chronicity and recurrence in suppurative otitis.

Postoperative Care.—Fifty cases in the early part of the series were compared with fifty cases late in the series, because the method of postoperative care differed so widely in the two periods. In the first series, open packing of the mastoid cavity with frequent irrigations with normal saline, peroxide, Dakin's solution et al., was the

rule. In the second group the wounds were flushed with saline, lightly packed with bismuth gauze, periosteum was approximated with catgut sutures, and the skin closed, save for a slight opening at the inferior margin, with silk. Further than this, a gauze wick was inserted to the opening in the drum. Mastoid packing was slowly withdrawn from day to day or entirely replaced in four days with a small rubber catheter extending to the mastoid antrum. The results are as follows:

1. Duration of aural discharge
   (a) Under active treatment ..... 8.9 days
   (b) Under passive treatment ..... 5.0 days
2. Duration of Postoperative care
   (a) Under active treatment ..... 41.0 days
   (b) Under passive treatment ..... 28.5 days

The statistics would indicate the desirability of less interference with the mastoid wound during the healing period. Probably of equal significance is the comfort of the patient when more passive postoperative methods are employed.

CONCLUSIONS

1. Surgical incision of the tympanic membrane lessens duration of pain prior to aural discharge, affords an opportunity to collect uncontaminated cultures from the middle ear cavity, shortens the total duration of the disease, facilitates a more timely operation and lessens the number of complications of acute purulent mastoiditis.

2. The most common organism to invade the mastoid process is the streptococcus hemolyticus.

3. Pneumococcus type 3 is a most dangerous organism to invade the mastoid bone. It is insidious in its course and more frequently than other organisms, gives rise to serious intracranial complications.

4. Paranasal sinus disease and the presence of infected adenoids and tonsillar tissue are two important factors in the primary etiology and in the chronicity and recurrence of mastoid infection.

5. Some time between the eighth and twenty-first days has been found to be the optimum time to operate upon an acutely infected mastoid bone.

6. A tempered noninterference policy in postoperative treatment of mastoiditis lessens the period of postoperative discharge and care and is easier on the patient.

HENRY FORD HOSPITAL

BIBLIOGRAPHY

1. Page, J. R.: Bacteriology of Acute Infections of Middle Ear and Mastoid. Arch. Otolaryng., 20:447-451 (Oct.) 1934.

2. Guthrie, D.: Early or Late Operations in Acute Mastoiditis. J. Laryng. and Otol., 48:400-407 (June), 1933.

3. Campbell, E. H.: Association of Acute Sinusitis and Acute Otitis Media in Infants and Children. Arch. Otolaryng., 16:829-844 (Dec.), 1932.

4. Fowler, E. P.: Incidence of Nasal Sinusitis with Diseases of the Ear. Arch. Otolaryng., 9:159-170 (Feb.), 1929.

LXXXIV

SUPRAGLOTTIC LARYNGEAL EDEMA: CHARACTERISTIC RESPIRATORY SOUNDS AS AN AID IN DIAGNOSIS

A. Harry Neffson, M.D.

New York

One of the most treacherous conditions to be found in the practice of medicine is that caused by edema of the supraglottic structures of the larynx—namely, the epiglottis, aryepiglottic folds and arytenoids.

When laryngeal stenosis is due to an inflammatory edema of the mucous membrane of the glottis and of the subglottic region, the respiratory difficulty usually grows greater gradually, with a progressive appearance of the signs and symptoms denoting increasing asphyxia. This manner of development gives the physician quite a wide margin of safety and permits him to wait for improvement with palliative measures before resorting to some form of mechanical relief of the obstruction. On the other hand, in patients with supraglottic edema the general appearance often belies the gravity of their condition. Thus, even with severe edema and impending asphyxia the patient may be quite comfortable, of good color, and have only moderate suprasternal, with little or no substernal, retractions during inspiration. The cyanosis or ashen pallor, the restlessness and anxious facies, and the deep retractions with greatly diminished breath sounds which are found in patients with glottic and subglottic edema of comparable severity are usually not seen with supraglottic edema. (The glottic and subglottic spaces being limited, edema results in immediate signs of obstruction; in supraglottic edema the tissues bulge into the pharynx so that obstruction may not occur until the swelling is extreme.) Because of this lack of distress the physician is led to feel that he can safely observe this patient just as he has other patients with "croup" in the past. Here lies the danger! With catastrophic suddenness the patient's condition may be radically altered. A fit of coughing or even a change in the position of the body may so displace the waterlogged, flabby supraglottic structures that they are suddenly drawn into the glottis or else a slight increase in the edema may quickly plug the lumen. With each succeeding frantic inspiratory effort the tissues are jammed down more tightly and the patient may become asphyxiated before help can be given.

It is evident that any sign which can be of help in making an earlier diagnosis of such a fatally deceptive condition is of vital importance.

During close observation of more than a thousand patients with "croup" of varying forms and etiology at the Willard Parker Hospital from 1930-35, a peculiar, stertorous respiration was noted in several patients with supraglottic edema. This was distinctly different from the muffled, high-pitched respiratory stridor heard in the usual type of laryngeal obstruction—that is, glottic and subglottic. This respiratory sound was so striking to the trained ear that thereafter the diagnosis of supraglottic edema was made repeatedly solely upon hearing it and each time it was confirmed by direct laryngoscopy.

As first described in a paper by Neffson and Wishik[1] this breathing is characterized by a "low-pitched inspiratory stertor with a louder and lower-pitched, coarse, expiratory rattle, resembling a snore." (By performing the act of gargling, with the mouth dry, and causing the relaxed tissues of the larynx and pharynx to vibrate for about one second, an idea of the sound of this coarse, expiratory rattle can be obtained.)

Because this was mentioned among many other facts it is felt that it did not receive the emphasis its importance merited. Moreover, since publication of the paper, some of our colleagues have confirmed this observation. Also, there have been seen several patients[2] with supraglottic edema in whom only the characteristic expiratory component was present—namely, a loud, low-pitched, coarse, expiratory rattle with either a somewhat muffled, high-pitched inspiratory stridor or no inspiratory stridor at all. In these cases, too, the diagnosis was made upon hearing the coarse expiratory rattle and was confirmed by laryngoscopy.

I have tried to duplicate this condition in the human larynx postmortem by injecting water into the supraglottic tissues and then applying suction and air pressure to the cut end of the trachea. With marked edema of the arytenoid and aryepiglottic fold on one side there was heard a low-pitched, coarse rattle during both inspiration and expiration caused by the vibration of the swollen tissues. In some instances, depending upon the location and severity of the swelling, a coarse rattle was heard only during expiration, the inspiratory sound being absent. When both sides were tremendously edematous there was a low-pitched, coarse rattle only during expiration. With inspiration the swollen tissues were drawn in toward the glottis, coming in close contact with each other and preventing vibration, thus causing a high-pitched, inspiratory stridor.

It is urged that when this peculiar expiratory rattle is heard the patient be laryngoscoped at once to confirm the diagnosis of supraglottic edema. Furthermore, when the diagnosis is established it is essential that the patient be watched constantly by one who can quickly insert a metal tube, such as a bronchoscope, if the need arises; otherwise, a tracheotomy should be done at once. Scarification and adrenalin sprays may be tried in adults if they are carefully watched; in children such measures are extremely dangerous because they are apt to become panic-stricken and be asphyxiated right under one's eyes. Intubation with an O'Dwyer tube is likewise extremely dangerous because the tube causes outward pressure on the swollen tissues with a consequent displacement of the edema upward and around the upper opening of the tube. Also, the inflamed tissues become irritated by the tube and are apt to swell even more, so that there is great likelihood of a sudden pulling-in of the tissues into the upper end of the tube with immediate asphyxia. Moreover, the knowledge that a tube is in the larynx may give the physician a false sense of security.

It is hoped that recognition of this unique type of stertorous respiration, which I believe to be pathognomonic of supraglottic edema, and the appreciation of its significance will enable the physician to take the necessary precautions for the patient's safety and help prevent sudden avoidable deaths from asphyxiation in this condition.

152 East 94th Street.

BIBLIOGRAPHY

1. Neffson, A. H., and Wishik, S. M.: Acute Infectious Croup: A General Study of Acute Obstructive Infections of the Larynx, Trachea, and Bronchi with an Analysis of 727 Cases. J. Pediat., 5:433 (Oct.), 617; (Nov.), 776; (Dec.), 1934.

2. Som, M. L., and Neffson, A. H.: A New Danger: Aspiration of Carbon Dioxide Snow. J. A. M. A., 108:970 (Mar. 20), 1937.

LXXXV

SEASONAL VARIATIONS IN BLOOD COAGULATION—A STUDY BASED ON 1676 CASES*

LLOYD K. ROSENVOLD, M.D.

LOS ANGELES, CAL.

AND

JOSEPH B. MILLER, B.S.

SAN JOSE, CAL.

For several years past, a number of clinicians at the White Memorial Clinic have noticed the apparent prolongation of the time for blood coagulation during the winter† months as compared with the summer months. In order to determine the accuracy of the above observation, the authors tabulated and studied the results of 1676 bleeding and coagulation time determinations done at the clinical laboratory by various technicians during the years 1935 and 1936. For the permission to study the laboratory records, we are greatly indebted to Dr. O. B. Pratt, pathologist of the White Memorial Hospital. Through the courtesy of the Los Angeles office of the Weather Bureau of the U. S. Department of Agriculture, we obtained meteorological data for the years 1935 and 1936, and this we have correlated with our findings in the accompanying graph.

The bleeding time was determined by means of capillary punctures of the ear lobes or fingers. The coagulation time determinations were done by the common "slide" method. Most of the individuals upon whom the determinations were made were otolaryngological patients who had been advised to have surgery of one form or another. The patients ranged in age from infancy to old age, with children and young adults predominating.

A search of the literature yielded very little information regarding seasonal or climatic effects upon blood clotting. Turnley[1] in discussing the various results of 76,000 adenoid and tonsil operations states

*From the Department of Otolaryngology, College of Medical Evangelists, Los Angeles, Cal.

†For purposes of convenience in this paper, we have divided the year into two seasons. One, the winter, lasting from November to March, inclusive; and the other, the summer (or summer months), embracing April to October, inclusive.

that: "There are more bleeding vessels to ligate at the time of operation during the summer months when the barometric pressure is low." Whether or not this is generally true we cannot state, but perhaps it is the case on the eastern seaboard where Turnley made his observations. Bähler[2] studied the effect of altitude on the blood platelets and blood coagulation of two persons (one male and one female) at altitudes of 673, 1277, and 3476 meters above sea level. No statement was made as to what time of the year the observations were made. From his report we conclude that as the higher altitudes are reached: (1) thrombocytes (platelets) are increased in number, (2) the clotting time is increased, (3) the bleeding time is shortened, and (4) retractility is diminished.

TABLE I

For the years 1935 and 1936

Month.	No. of cases.	Bleeding time in minutes.	Coagulation time in minutes.
January	93	2.65	5.01
February	104	2.50	3.90
March	134	2.65	5.02
April	123	2.80	3.82
May	124	2.77	4.19
June	155	2.91	3.70
July	209	2.65	4.08
August	270	2.54	3.27
September	176	3.11	4.10
October	129	2.80	3.80
November	95	2.70	5.80
December	64	2.60	4.98

Coagulation Time.—From Table I it will be seen that the higher average figures for the clotting time were recorded during the winter months, whereas the lower average figures were recorded during the summer months. The two year average is strikingly illustrated in the accompanying graph.*

The average coagulation time for the 1186 cases recorded in the summer time was 3.751 minutes, whereas the average for the 490 winter cases was 4.918 minutes. It is, therefore, evident that the average coagulation time for the winter months exceeds that of the summer months by 1.167 minutes or about 70 seconds. We are of

*When we plotted curves for each year separately, we found that the general trend of both curves was the same. The same is true of the meteorological curves. For that reason, the corresponding months of the two years were averaged into one, i. e., January, 1935, and January, 1936, averaged together, etc.

the opinion that this difference is great enough to be of definite significance.

Bleeding Time.—It will be noted that even though bleeding time determinations are notoriously subject to error (differences in site, type, and size of puncture), the average bleeding times for the various months were fairly constant. In fact the difference between the shortest and longest monthly averages is only 0.61 minutes or about 36 seconds, and the summer average is only nine *seconds* longer than the winter average.

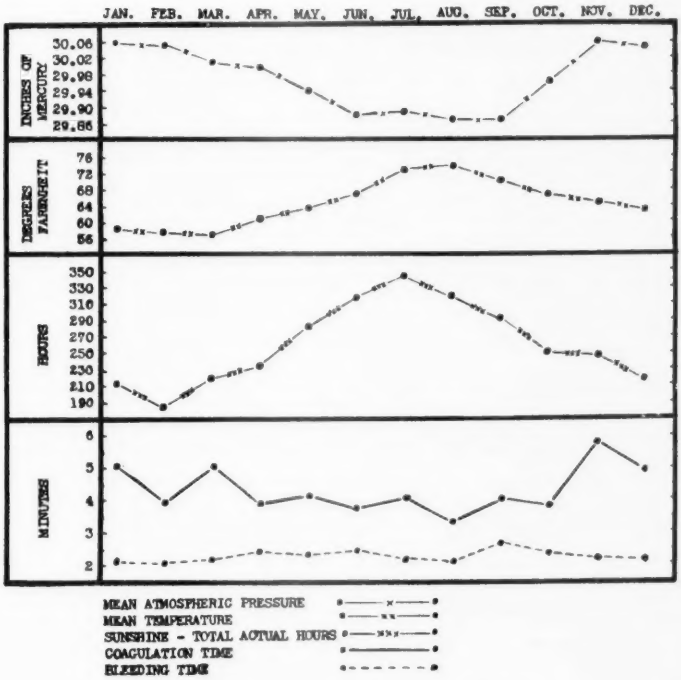
COMMENT

In an effort to explain the seasonal variation in coagulation time that we detected in our series, we have plotted on the same graph, curves representing the various meteorological conditions as they occurred in Los Angeles during 1935 and 1936.

Atmospheric Pressure.—The curve for atmospheric pressure in general parallels the clotting time curve. Our study indicates no support for the statement of Turnley[1] that there are more bleeding vessels in the summer time when the barometric pressure is low. In our city, the greatest difference in pressure between any two months as noted on the graph was only 0.19 inch or about 4.8 mm. of mercury. It is difficult to conceive how this small variation in pressure might be sufficient to influence blood coagulation or bleeding time values.

Temperature.—The temperature curve inversely parallels the coagulation time curve. We are not of the opinion that the surrounding atmospheric temperature directly influenced blood clotting.

Hours of Sunshine.—The curve for total actual hours of sunshine also inversely parallels the coagulation time curve in a general way. Phillips et al[3] studied the effect of feeding irradiated ergosterol to a large series of rats. They found a rather marked increase in thrombocytes and a decrease in coagulation time of the blood. Sanford[4] in 1927 studied 50 newborn infants using half as controls. He found that short exposures to ultraviolet light lowered the bleeding time, increased the platelets temporarily, but did not affect the clotting time. However, in 1932 Sanford[5] and his co-workers stated after studying twenty healthy newborn that, "Either exposure to ultraviolet radiation or the administration of viosterol 250 D, or both, will, in the newborn, tend to increase the fibrinogen of the coagulating substance to a slight extent, and to decrease the antithrombin, thereby increasing the tendency for the blood to clot."



Graph showing averages for 1935 and 1936

Brougher[6] reports seven cases with prolonged clotting time each of whom were given one ounce of cod liver oil and the clotting time repeated four hours later. The average clotting time for the series was reduced from 17 minutes to 5 minutes (Lee and White). Another series of similar cases was given ten drops of viosterol orally and the clotting time determinations repeated in four hours. The average clotting time was reduced from about 14.5 minutes to 8.5 minutes. All of Brougher's cases were suffering from some infectious or systemic disease and a number had syphilis.

Since ionic[7] or ionizable[8] calcium is essential for blood coagulation and since vitamin D is so intimately connected with calcium metabolism, the question arises as to what rôle calcium played in the above experiments with vitamin D. Reed and Tweedy[9] found that direct irradiation of blood in vivo with a carbon arc does not produce

any immediate change in blood calcium in dogs under ether anesthesia. Thus Broughers results were possibly not on the basis of an increased blood calcium.

It would appear on the basis of the literature reviewed that the decrease in the coagulation time during the summer time as noted in our series could be due to the increased amount of sunshine (and consequently increased amount of vitamin D) available during the summer months. It is the only probable meteorological explanation that we have found.

Though vitamin C, which is known to influence clotting and bleeding, is abundant in the citrus fruits of southern California, we do not believe that it was of much seasonal influence in our series since the fruits are available at all times of the year.

Further Research.—Obviously the study of a problem from records compiled in the course of routine work is not as satisfactory as study planned with definite factors of control in mind. A more ideal method to approach the problem would be to study a large group of volunteers at definite monthly intervals and at a set hour of the day each time so that the meals[10] would not alter the coagulation time. Besides making clotting time determinations, other physical and chemical blood tests that have a bearing on blood coagulation should be made. Meteorological data as furnished by the U. S. Department of Agriculture should also be correlated with the experimental findings. Studies of this kind, carried out in different climatic and geographical situations would greatly further our present knowledge of the subject at hand.

SUMMARY

The seasonal variations in blood coagulation have been studied from the records of 1676 patients and covering a period of two years.

Meteorological data has been correlated.

The much disputed question[11] of the relative value of preoperative coagulation time determinations in otolaryngology is not discussed in this paper.

CONCLUSIONS

1. The coagulability of the blood as determined by the slide method is decreased during the winter months in southern California (Los Angeles County).

2. This would seem to favor doing elective surgery of the nose and throat during the summer time.

3. The bleeding time does not vary appreciably with the seasons.

4. Further studies in this field are indicated.

COLLEGE OF MEDICAL EVANGELISTS.

REFERENCES

1. Turnley, Wm. H.: The Results of 76,000 Adenoid and Tonsil Operations. Laryngoscope, 47:1 (Jan.), 1937.

2. Bähler, H.: Ueber den Einfluss des Hochgebirgsklimas auf die Blutgerinnung und auf die Zahl der Blutplättchen. Schweizerische medizinische Wochenschrift, 66:460 (May 9), 1936.

3. Phillips, R. A., Robertson, D. F., Corson, W. C., and Irwin, G. F.: The Effect of Irradiated Ergosterol on the Thrombocytes and the Coagulation of the Blood. Ann. of Internal Med., 4:1134 (March), 1931.

4. Sanford, H. N.: Effect of Ultraviolet Light on the Blood of Newborn Infants. Amer. J. of Dis. of Children, 33:50 (Jan.), 1927.

5. Sanford, H. N., Gasteyer, T. H., and Wyat, Lois.: The Substances Involved in the Coagulation of the Blood of the Newborn. Amer. J. of Dis. of Children, 43:566 (March), 1932.

6. Brougher, J. C.: The Effect of Vitamin D on Blood Coagulation Time. Northwest Med., 29:38 (Jan.), 1930.

7. Wöhlisch, E., and Paschkis, K.: Calcium and Thrombin. Klin. Wochenschr., 2:1930 (Oct. 15), 1923. Abstr. J. A. M. A., 82:72 (Jan. 5), 1924.

8. Smith, C. H.: Studies in Calcium and Blood Coagulation. Am. J. Med. Sciences, 169:572 (April), 1925.

9. Reed, C. I., and Tweedy, W. R.: Studies on the Physiological Action of Light. VII. Blood Calcium in Direct Irradiation of Blood. Amer. J. of Physiol., 76:54 (March), 1926.

10. Cowan, D. W., and Wright, H. N.: The Interrelationship between Blood Sugar, Blood Calcium, and Blood Coagulability. Amer. J. of Physiol., 100:40 (March), 1932.

11. Hunt, W. M.: Coagulation Time Prior to Tonsillectomy. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 36:187 (March), 1927.

LXXXVI

CLINICO-PATHOLOGICAL OBSERVATIONS OF OTITIS MEDIA AND PARATYMPANITIS*

LYLE M. SELLERS, M.D.

DALLAS, TEXAS

In 1932 we published a preliminary report concerning observations on suction treatment of otitis media in 150 consecutive cases.[1] At that time we stated that certain anatomical and pathological phases of a more detailed study were under way, and that a further report of these studies would be forthcoming.

This communication constitutes that report, together with further clinical observations of the continued use of the treatment in 300 consecutive cases.

The method of treatment is not new. It has been advocated by many[2, 3, 4, 5, 6] and it has been condemned by others. Those who condemn it do so because they feel that it is useless, because the surrounding bony walls are unyielding and therefore do not permit of aspiration; or that it is dangerous; or that it is painful. The first and last of these objections may be dismissed promptly. Those who doubt the possibility of aspiration have only to watch it occur by means of the Siegle otoscope. Any pain that may occur during its use is negligible in comparison to that of a neglected otitis media —especially the complications thereof—and may be minimized by care and gentleness. The final objection of danger will be dealt with more fully in discussing the technique of its application and in the analysis of certain of the cases observed.

ANATOMY AND PATHOLOGY

Our discussion is predicated on recognition of the fact that acute purulent otitis media (aside from such unusual cases as may

*From the Department of Otolaryngology, Baylor University School of Medicine, Dallas, Texas.

Photography and photomicrography by Lewis Waters of The Department of Medical Art, Baylor University School of Medicine.

The study of the microscopic anatomy and pathology necessary to the completion of this work was made possible through the courtesy of Dr. Lee Wallace Dean and Dr. Dorothy Wolff, who kindly placed the microscopic specimens of the Department of Otolaryngology at Washington University at our disposal, and who graciously allowed their use for photographic reproduction.

follow trauma or otitis externa) results from infection ascending from the upper respiratory tract.

Until quite recently the concept generally held was that such infections ascended the lumen of the eustachian tube much as smoke ascends a flue.

We now must recognize that there are at least three routes by which such infections may travel from the respiratory tract to the middle ear and its adnexa. To these structures we will henceforth apply the terms suggested by Linck—the tympanum and the paratympanum.[7] The route followed is of prime importance because its plays a most important role in determining the clinical type of otitis media that results, there being three distinct such types. It may be stated that certain types of bacteria may show predilections for certain routes. This hypothesis we presented in two papers read in 1935[8, 9]. It was demonstrated microscopically for the first time by Hadjopoulos and Bell[10] in 1937.

To understand the mechanism underlying these three routes let us first observe quite briefly the embryologic development of the temporal bone cavities, the tympanum and paratympanum. These cavities and their contained structures are developed from the structures of the first embryonic gill.

From the gill cleft lined by ectoderm come the lining of the external auditory canal and the outer (epithelial) layer of the tympanic membrane.

From the gill pouch lined by entoderm come the mucosa of the eustachian tube, tympanum, and paratympanum, and the mucosal or inner layer of the tympanic membrane.

From the arches and the surrounding mesoderm come the temporal bone and the footplate of the stapes, the arches of the stapes and the malleus and incus with their muscles and ligaments, the middle layer of the tympanic membrane, and the submucosa with its blood vessels, lymph spaces and channels.

The cavities representing the atrium, attic, antrum, and mastoid cells develop by a process of osteoclastic absorption. This absorption of bone and cartilage is followed by expansion and out-pouching of the entodermal (mucosal) layer. In the fetus, and even in the new born, the submucosa is quite thick, as the oncoming mucosal layer has not been allowed to keep pace with the osteoclastic absorption. But very soon the excessive mesenchymal tissue within the submucosa resorbs, and in the course of normal development the

submucosa of the adult becomes very thin so that the mucosa lies in fairly close contact with the bone (Fig. 1h).

But in certain cases the submucosa fails to resorb properly. Wittmaack[11] considers such failure of resorption to be a result of prenatal inflammation of the middle ear, probably from invasion of the region by amniotic fluid. But whatever its cause, its presence serves to aid in propagation of certain types of otitis media, and markedly retards recovery when an otitis has been established. It is very important that such a condition be recognized clinically when it occurs (Fig. 2).

We will now consider the three routes of infection with the three types of acute purulent otitis media that they produce.

Type I.—Infections reaching the middle ear via the lumen of the tube are usually quite mild. Their behavior varies according to the age of the patient and the virulence of the infecting organism.

These infections are most frequently found in the infant because of its short, patent, horizontally placed tube.

If the infecting organism is mild, the tympanum acts only as a reservoir for the secretion which is usually of a mucoid or mucopurulent type (Fig. 3). The child is not clinically ill, at worst showing only slight restlessness and a very low grade elevation of temperature. Frequently the condition is found during the course of a routine clinical examination with no symptoms even suggesting an otitis media. Here the membrane is smooth and pale, and the landmarks are blurred or there is slight bulging. The outcome usually is complete restoration of structure and function with neither rupture nor myringotomy.

But if the infecting agent be virulent and if myringotomy be delayed, ulceration and necrosis of the mucosa occur and the course then follows that of type III.

In the adult the infective agent usually is forced through the longer and narrower tube by nose blowing or sneezing during an acute upper respiratory infection. The only subjective sign may be a fullness and discomfort in the ears. Examination discloses a pale or pale red blurring of the drum head which, as in the infant, quickly resolves itself or, if the infection be virulent, invades the submucosa and otitis media of type III follows.

Type II.—In discussing types II and III we must refer again to the epochal work of Hadjopoulos and Bell. They feel that milder and more localized infections result from superficial invasion of the

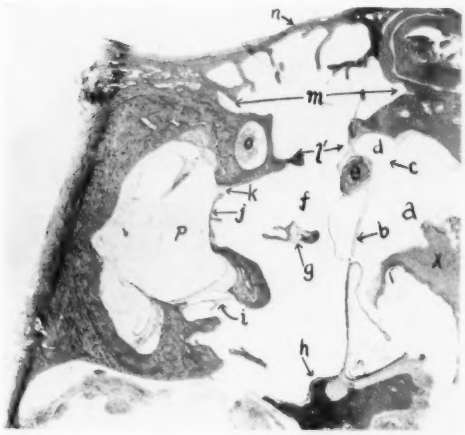


Fig. 1. Frontal section through the middle ear and vestibule of the infant showing complete development with very thin submucosa.

a. External auditory canal.
b. Tympanic membrane.
c. Shrapnel's membrane.
d. Prussak's space.
e. Short process of malleus.
f. Middle ear space.
g. Incudo-stapedial joint.
h. Mucosa with thin submucosa.
i. Round window and membrane.
j. Foot-plate of stapes.
k. Annular ligament of stapes.
l. Constriction between attic and atrium.
m. Attic at widest part.
n. Tegmen tympani.
o. Facial nerve.
p. Vestibule.
x. Loose tissue in external canal.

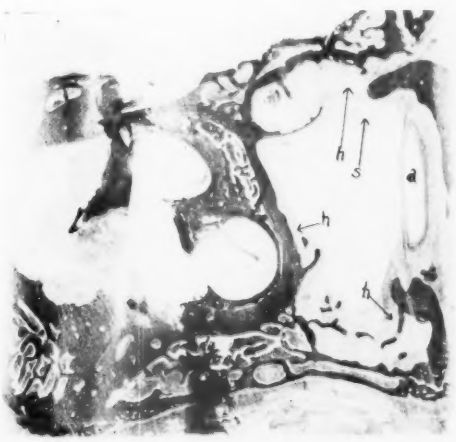


Fig. 2. Frontal section through the anterior portion of the middle ear of the infant, showing moderate hyperplasia of the submucosa and a mild type III otitis media.

a. External auditory canal.
h. Hyperplastic submucosa.
s. Exudate clinging to the mucosa.

submucosa, and that the severer and more extensive infections result from invasion of the deeper layers of the submucosa with propagation of the infecting organisms by the lymph channels and venous capillaries. We feel from the clinical evidence at hand that further differentiation must be made. In our communications previously referred to[8, 9] such differentiation was made. We hope that they will offer more concrete experimental evidence of this. This differentiation is herewith presented.

Type II is fortunately the rarest as certainly it is the severest and most dangerous type. Here progress is via the blood vessels, and we must recognize at least two sub-types, the true hemorrhagic and the thrombotic.

The true hemorrhagic type recognized by Kopetzky,[12] caused by innumerable and multiple thrombi, is explosive in onset. All structures related to the middle ear are invaded simultaneously and extensive necrosis occurs with lightning-like rapidity. Myringotomy offers little or no relief and the course is rapid, progressive and severe in spite of active treatment. The patient is patently and dangerously ill. One typical case seen by me became ill on a Saturday. Myringotomy was performed promptly. On the following Tuesday I saw the patient for the first time. He had characteristic septic temperature; severe tenderness and edema of the mastoid and surrounding area; a bloody otorrhea yielding approximately one ounce per hour; and the blood count showed a total white count of 8,000, polynuclear count 76 per cent, band forms 48 per cent and multilobed forms 28 per cent. Mastoidectomy performed on Thursday disclosed numerous areas of extensive necrosis with hemorrhage from the intervening areas. The sinus plate and the tegmen zygomatici were necrotic and the dura and sinus were thickened and inflamed. Cultures from the ear and mastoid yielded streptococcus hemolyticus.

All such cases are inevitably surgical.

The thrombotic type presents areas of necrosis (many times lying at a distance from the antrum and from each other) representing the degenerated products of infarcts. Between these areas normal tissue may be found completely separating them. This should negate the thesis that they are the result of spread by continuity of tissue.

The symptoms, particularly the systemic symptoms, are not as severe as those of the true hemorrhagic type unless the larger venous channels are invaded. In a recent article, Greenfield[13] includes two such cases in a list of cases of lateral sinus thrombosis.

Fig. 3. Frontal section of the middle ear of the infant, showing a mild type I otitis media.

s. Exudate clinging to the mucosa.
h. The very slight hyperplasia of the submucosa.
f. The atrium.
t. The beginning of the horizontal semicircular canal.
s'. Exudate within Prussak's space. This exudate with the edema of Shrapnel's membrane extending downward over the short process of the malleus graphically explains the blurring of the landmarks in such cases.

Fig. 4. Frontal section of the temporal bone through the external auditory canal and the anterior half of the middle ear (See also 1 in Fig. 5).

1 -1'. The great width of the communication between the attic and the atrium usually seen in text book illustrations. Here the attic appears as an open bucket inverted over the internal opening of the eustachian tube.
w. The internal opening of the eustachian tube.

Abortive treatment is usually unavailing and operative relief is required. Supportive treatment is indicated until evidence of local reaction is sufficient to assure safety in operation, or until it is evident that the patient is unable to react, as in the case cited above.

Type III.—In this type the route of invasion lies along the intercellular spaces and lymph channels of the submucosa. We feel that this route produces the cases of serous and purulent otitis media usually encountered. These cases when they do not resolve, result in the type of mastoiditis called by Kopetzky[12] the coalescent type or in so-called chronic purulent otitis media.

Proper treatment of this type of case must be based on the recognition of a structural arrangement of the tympanum and paratympanum, and certain consequent pathological processes apparently not previously described.

Usual text book pictures of frontal sections of the attic show it as an inverted open bucket, wider below than above, and draining downward into the eustachian tube which opens like a funnel below it (Figs. 4-5). This arrangement is true only if the section is through the anterior half of the structure and at an angle sloping from behind and above, somewhat downward and forward.

If the section is made through the posterior half, the cavity of the attic is seen to be shaped like an inverted truncated cone (Figs. 5-6). If the tympanic membrane is intact the cavities of the tympanum and attic together have roughly the shape of an hour glass. In this region lie the ossicles with their ligaments, the tendon of the tensor tympani, the folds delimiting Prussac's space, and the chorda tympani (Fig. 7). The partially obstructed bottle neck thus formed is of prime importance. (R. R. Woods[14] in his recent monograph has described the frontal section of the attic as being a truncated inverted wedge but he fails to call attention to the difference between the shape of the anterior and posterior sections. Tremble[15] and others have noted the triangular shape of the antrum but do not mention the truncated cone shape of the posterior half of the attic.)

Above the ossicles lies a free space with its long axis in a direction from postero-lateral to antero-medial (Fig. 6). The axis has been designated by Ballance[16] the antro-tympano-tubal axis. We will designate the space lying in this axis the antro-tubal drainage way. In health or in mild catarrhal infections the antro-tubal drainage way suffices to drain the tympanum and paratympanum.

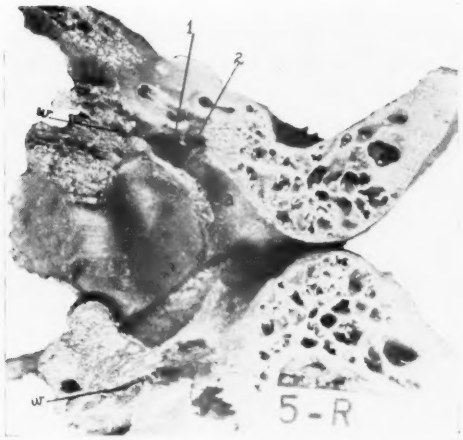


Fig. 5. Horizontal section of the temporal bone through the external canal and middle ear.

1. Looking upward into the attic through the wide anterior portion.
2. Looking upward into the attic through the narrow constricted posterior portion.
a. External auditory canal.
w. Internal opening of the eustachian tube.

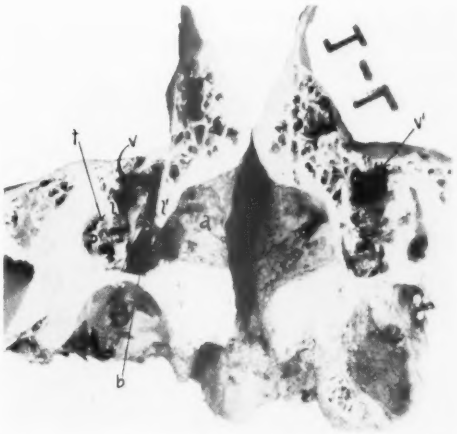


Fig. 6. Frontal section through the temporal bone through the external auditory canal and the posterior half of the middle ear (See also 2 in Fig. 5).

a. The external auditory canal.
1-1'. The constriction between the attice above and the antrum, giving to the attic the form of an inverted truncated cone. Note the facial nerve lying just below 1 and giving an even greater constriction at this point than is at first apparent in the photograph.
v. The antro-tubal axis drainage way leading forward toward the eustachian tube. Just under the arrow is the superior suspensory ligament of the malleus.
b. The tympanic membrane.
p. The vestibule.
t. The beginning of the horizontal semicircular canal.
v'. The antro-tubal axis drainage way looking backward into the antrum.

But with the onset of a severer process this drainage way becomes blocked by edema in the region of the malleo-incudeal joint. Under favorable conditions (especially in the mild cases of type I) this edema may limit the process to the anterior half of the atrium and attic giving rise to a mild anterior otitis media with possibly an anterior perforation of the tympanic membrane.

If the process is more virulent and if the posterior half becomes actively involved this blocking prevents direct drainage of the posterior region via the antro-tubal drainage way (Fig. 8), and the drainage route is detoured via the constricted and partially obstructed cone-shaped posterior half to the atrium. The edema and infiltration of the submucosa increase, and the integrity of the mucosa is interrupted so that ulceration occurs with consequent out-pouring of serum and pus. This exudate can escape from the attic to the atrium only via the detour drainage route.

Here the structural arrangement predisposes to stagnation of the exudate with deposition of pus cells and granular fibrin. This produces plugging of the already narrowed and obstructed detour (Fig. 9). The exudate then dams back to the exits of the antrum and mastoid cells with their rigid, bony walls creating within these spaces additional edema from negative pressure as the contained air is absorbed. In the meantime the granular fibrin in the bottle neck becomes fibrillar; there is an invasion by newly formed blood vessels, and increased proliferation of tissue occurs (Figs. 10-11-12-13).

Should this process reverse itself healing occurs; but if it progresses acute coalescent surgical mastoiditis develops. Should healing then be attempted fibrosis of the proliferative tissue begins and the result is that chronic purulent otitis media or mastoiditis develops (Fig. 14).

THE PROBLEM

Consideration of our problem reveals now that we must think in terms of double drainage. By this we mean first that simple incision of the tympanic membrane with drainage of the atrium is insufficient. The emergency detour drainage way, narrow and constricted at its best, must be kept as open and free as possible so that exudate may be led safely and promptly from the antrum and attic to the atrium, and that air be allowed to find its way to the upper posterior recesses as the exudate is displaced. From the atrium gravity will allow the exudate to escape into the external auditory canal if the incision is kept patent and free of foreign body obstruc-

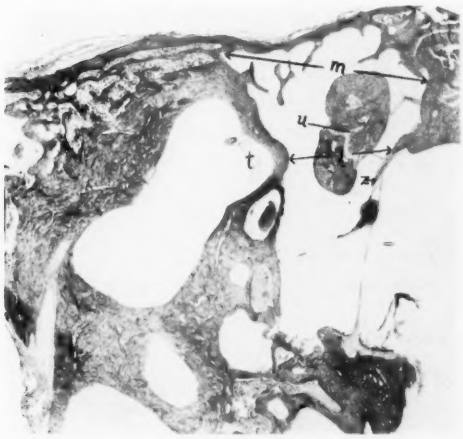


Fig. 7. Photomicrograph of a frontal section through the middle ear at approximately the same region as the gross section shown in Fig. 6.

t. The beginning of the horizontal semicircular canal.
m. The attic at its widest part.
l. The constricted narrow communication between the attic and the atrium. Laterally the constriction continues inward and downward to the point z.
u. The malleo-incudeal joint. Here the bodies of the malleus and incus partially obstruct the drainage way much like a modified ball valve.

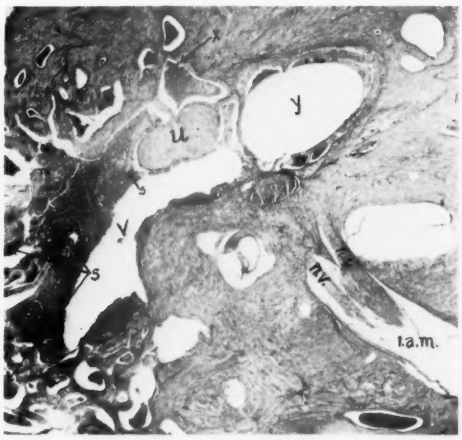


Fig. 8. Horizontal section through the attic of a patient suffering from acute purulent otitis media (Type I severe).

i.a.m. The internal auditory meatus.
n.c. The nervus cochlearis.
n.v. The nervus vestibularis.
y. The anterior half of the attic.
v. The posterior half of the attic and the antrum.
u. The malleo-incudeal joint. Here it may be seen how the ossicles and associated structures block the antro-tubal axis drainage way. Compare the scant amount of secretion in the comparatively open anterior half with the exudate s. that is dammed back into the antrum and on back into the mastoid cells.
x. Area enlarged in Fig. 13.

tion. Second we must strive to re-establish as promptly as possible the normal patency and function of the antro-tubal axis drainage way.

In an effort to solve this problem we have used the following procedure in our series of 300 cases. The results that we have obtained warrants this report.

TREATMENT

First.—Wide incision of the drum head at the point of greatest bulging, as soon as the presence of exudate is diagnosed, but not earlier.

Since the bulging is usually posterior, we prefer a hook-shaped incision beginning just anterior to the umbo, then circling under it and then running high up posteriorly. By a doughy feel of the tissues as the knife progresses we may detect the presence of a persistently thickened and edematous submucosa. The canal is mopped repeatedly until active bleeding ceases, when a gauze wick is inserted until it lies well within the gaping incision. Instructions are given to remove this wick at the end of two hours at which time any clots that may have formed will have become enmeshed in the wick and will come away with it.

Second.—Cleansing of the canal.

As soon as the wick is removed the canal is douched with sterile boric acid solution. Since the purpose of this douche is to keep the canal and external surface of the drum head free of debris, we feel that it is best accomplished with the ordinary ear and ulcer syringe, a firm, steady pressure being applied with the hand. Should fibrin or clots form they are dissolved with hydrogen peroxide. The douching is repeated every two hours unless the patient is asleep. The patient is instructed to keep the affected ear dependent as much as possible to facilitate drainage from the canal by gravity.

Third.—General care.

The patient is kept in bed until the temperature has returned to normal. For the first thirty-six or forty-eight hours, or until the tenderness subsides, ice is applied to the mastoid. Astringent antiseptic drops are used in the nose, and blowing of the nose is prohibited as long as the perforation remains patent. The throat as well as the nose is freed from infection as soon as possible, for the ear will rarely recover if either remains infected. Rest and ease from pain are sought by the use of simple anodynes. We have not

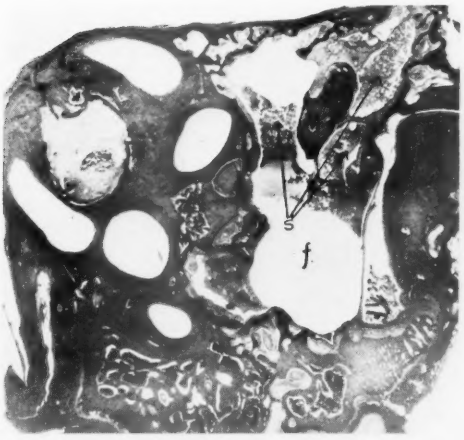


Fig. 9. Frontal section through the posterior half of the middle ear of a patient suffering from acute purulent otitis media type III.

f. The atrium.

s. Exudate being forced through the constriction of the detour drainage way. It is being dammed back into the upper recesses by the ossicles and associated structures. Contrast this section and the section shown in Fig. 10 with Fig. 2. All three are from the same patient. They clearly illustrate the ease with which the anterior half drains itself and the obstruction to drainage and the consequent difficulty of drainage via the posterior detour.

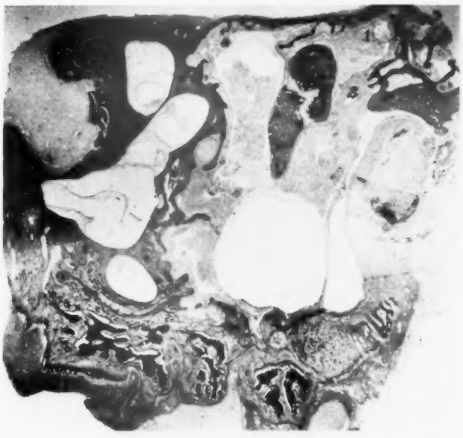


Fig. 10. Frontal section through the posterior half of the middle ear of a patient suffering from acute purulent otitis media, type III. Although from the same patient shown in Fig. 10, the process at this level is more advanced, showing two stages of organization of the exudate. (Photomicrograph previously published in ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 40:1055 (Dec.), 1931.

1. The area shown in Fig. 11.

2. The area shown in Fig. 12.

as yet had sufficient experience with the use of sulfanilamide to discuss it at this time.

Fourth.—Drainage of the upper spaces via the detour drainage way.

The patient is seen daily until the infection has been cured. At these daily treatments the canal is thoroughly cleansed. Then a Siegle type otoscope is inserted, and under direct vision gentle suction is applied. The amount of negative pressure required varies with the patient and the severity of his reaction to the infection. But as long as the procedure is carried out under direct vision with an ordinary No. 4 rubber bulb as the source of negative pressure, no untoward results are to be feared. These simple precautions will overcome completely the objections mentioned earlier of those who fear damage to the vital structures of the ear. At this time one condition, if present, must be recognized if it has not been recognized previously. That is the presence of an excessively thickened submucosa. If this is present, suction must be used with unusual caution or increased edema with consequent delay in healing will result. This happened in two of our cases before we learned to recognize the condition. For the first few days a gush of blood immediately follows the application of the negative pressure and completely obscures the drum. This is wiped away and the suction repeated until assurance is given that there is free drainage. A wick is introduced and instructions are given for home care as before.

After the second or third day the character of the discharge changes to a yellowish serous or purulent type. Following several applications of the mild suction a bloody discoloration seen to come only from the region of the attic tinges this discharge, after which no further suction is used at that treatment. After the third or fourth day the bloody tinge usually disappears and suction may be continued as long as deemed necessary.

By this means pus and granular fibrin are dislodged from the bottle neck before organization occurs; aeration of the upper recesses is accomplished by displacement of the exudate; and early vascular invasions of any organizing masses are ruptured, as evidenced by the blood tinging of the exudate from the attic. In the later stages healing is probably aided by the development of passive hyperemia.

Fifth.—Drainage and re-establishment of the antro-tubal axis drainage way.

During each daily treatment the nose is inspected and all free secretion is removed with a small (capillary) suction tube. With

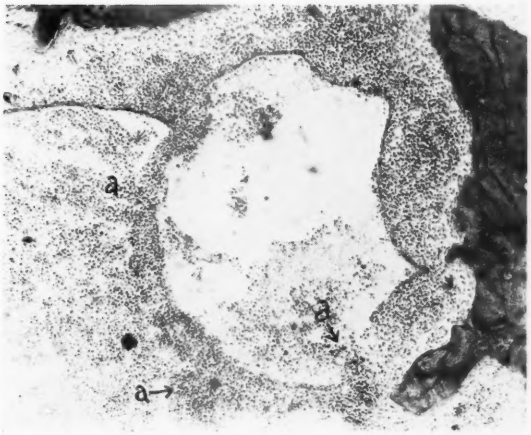


Fig. 11. This is the area shown in Fig. 10, 1. It is under very high magnification. It shows deposition of granular fibrin in the exudate and its invasion by embryonic connective tissue cells from the hyperplastic submucosa. Here is the beginning of adhesions with future permanent changes in the middle ear and mastoid.

a. Areas in which the invasion is occurring.

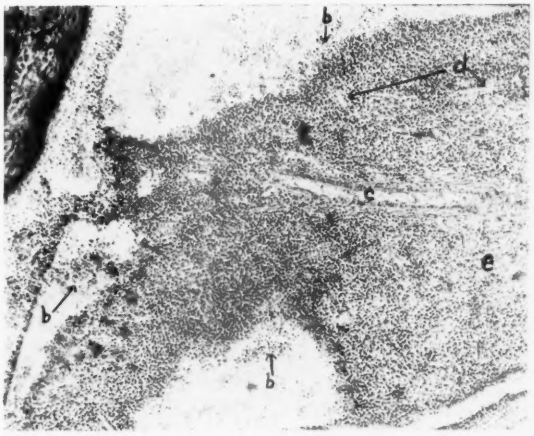


Fig. 12. This is the area shown in Fig. 10, 2. It is under very high magnification. Organization has proceeded far beyond that shown in Fig. 11. Here spindle cells are matting themselves across the area and blood vessels are invading the tissue. The embryonic connective tissue cells are here reaching out into the granular fibrin, thus increasing the extent of the blocking and later adhesions.

b. Outstreaming of the connective tissue cells into the granular fibrin.

c. New formed blood vessel lined by a single layer of endothelium.

d. Less mature blood vessels.

e. Long strands of maturing connective tissue.

the opposite nostril held closed, negative pressure is then applied to the nostril of the affected side through an olive-shaped nasal tip. During the application of the negative pressure, the patient is instructed to swallow (in infants crying suffices) in order to raise the palate with consequent simultaneous closure of the naso-pharynx and opening of the tubal orifice. By means of this reverse Politzerization we assist in immediate drainage of the anterior half of the paratympanum; we assist and reinforce the results obtained in the posterior half by the negative pressure applied to the external canal; we re-establish the patency of the tube, and we aid in re-establishing the permanent antro-tubal axis drainage way.

REPORT OF CASES

Our final series consists of three hundred consecutive cases covering a period of twelve years. This carries us through periods of various prevailing infections and climatic conditions. The cases were seen privately and complete records are available. No selection of cases was made except that each case must have been under our care from the approximate onset of the illness until its conclusion. Thus the series includes all types of cases with varying concomitant affections. Many such conditions prolonged the illness far beyond the general average thus greatly increasing the average period of convalescence. For example, two of the ulcerative hemorrhagic cases required packing for a number of days and the time required for healing of the extensively destroyed membrane was forty-seven and twenty-four days, respectively.

Although exact data concerning each case is in our possession, we present only summaries and digests at this time.

Table I presents an analysis of the cases by the year.

Yearly Incidence.—The year 1929 produced the greatest number of cases, nearly twice the number in any other year. We can assign no reason for this except the unusually large number of colds shown by our records.

Seasonal Incidence.—An overwhelming number of cases (180 or 60 per cent of the total) occurred during the winter-spring season (January to April, inclusive). This was to be expected, as we have the greatest number of upper respiratory infections during this season. Conversely the summer season (May to September, inclusive) produced the fewest number of cases (47 or 15.6 per cent).

Duration.—The duration of the illness—from the onset of the symptoms until cessation of the discharge and healing of the per-

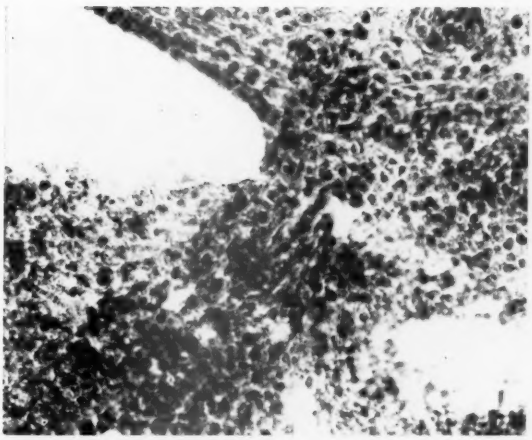


Fig. 13. This is the area marked "x" in Fig. 8 under highest dry power magnification. It is similar to the areas in Figs 11a and 12b. Here we see the immature connective tissue cells streaming from the submucosa at the upper right into the mass of organizing granular fibrin at the lower left. Because there are so few such areas in this case and because the submucosa shows so little reaction, healing probably would have occurred. In this respect this case differs from that shown in Figs. 11 and 12.

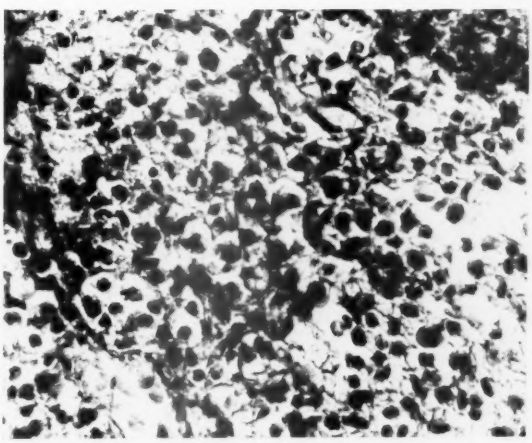


Fig. 14. This is a section of tissue removed from the mastoid of a patient who had suffered from infection of the mastoid for several years, but which had begun after the development of the mastoid was completed. It was not a sclerotic mastoid which results from failure of the mastoid to develop. The structure of this tissue shows its close relation to the tissue in Fig. 13. It is an end product of the process shown having its beginning in Fig. 13.

TABLE I

Year	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	Totals
Total Number	8	17	18	61	31	25	32	25	18	28	23	14	300
Winter-Spring	7	5	13	32	23	11	12	18	10	21	16	12	180
Summer	1	3	1	14	3	8	5	1	3	3	3	2	47
Fall-Winter	0	9	4	15	5	6	15	6	5	4	4	....	73
Ave. Duration of Illness	10.3	8.3	15.3	10.6	11.4	11.2	10.6	10.0	11.7	11.5	12.4	10.6	11.1
Ave. Duration of Treatment	9.4	6.9	13.	10.4	8.	10.	9.1	9.5	9.	9.8	11.3	7.5	9.6
Etiology													
Common Cold	4	4	8	45	23	16	22	12	12	13	12	7	178
Influenza	4	5	6	7	5	3	4	2	2	15	7	4	64
Tonsillitis	1	1	....	2	3	2	3	3	1	....	3	....	19
Measles	....	....	....	3	1	....	....	6	....	....	....	....	10
Otitis Externa	....	....	2	....	....	....	1	1	....	....	1	....	5
Scarlet Fever	....	1	....	1	....	....	....	....	....	....	1	....	3
Sinusitis	1	....	....	1	1	1	1	1	3	4	1	4	19
Pneumonia	1	....	2	1	....	....	2	....	....	2	....	....	8
Acute Lymph. Leukemia	....	....	....	1	....	....	....	....	....	....	....	....	1
Pertussis	....	....	....	....	2	....	....	....	....	....	....	....	2
Chicken Pox	....	....	....	....	....	2	....	....	....	....	....	....	2
Pharyngitis	....	....	....	....	1	....	....	....	2	....	....	....	3
Diphtheria	....	....	....	....	....	....	....	....	2	....	....	....	2
Trauma	....	....	....	....	....	2	....	....	....	....	....	....	2
Spont. Painless Rupture	....	....	....	....	....	1	....	....	....	....	....	....	1
Unknown	....	6	1	2	....	2	1	....	....	....	1	....	13

foration, or until it was determined that a permant perforation would remain—and the duration of the treatment ran a fairly uniform yearly course except for the year 1928. Here the duration was unusually long. The cause for this prolongation lies in the small total and the comparatively high incidence of influenza, pneumonia, and otitis externa as etiological factors.

The average duration of illness in all cases was 11.1 days and the average time required to affect a cure from the beginning of active treatment was 9.6 days. This is the average of all cases, both simple and complicated. The duration of the average case is actually much shorter. This comparatively short duration stands in marked contrast to the usually accepted figures. Kerrison[17] states: "In a favorable case, the discharge may cease and the drum membrane close in a period varying from ten days to four weeks." Wittmaack[11] states that in the simplest cases (without marked hyperplasia of the submucosa) the duration is two to four weeks.

Etiology.—As the prime etiological illness the common cold accounted for more than all other illnesses combined (178 or 59.3 per cent). Influenza was the next most frequent cause (64 or 21.3 per cent). Acute tonsillitis and acute sinusitis accounted for the same number each (19 or 6.3 per cent). Measles accounted for 10 or 3 per cent.

Otitis externa, strangely enough, for one seldom finds it listed as a cause, accounted for five cases. These cases were apparently truly otitis externa. But we must pause and consider that the locus in the external canal may have been, in at least one case which progressed to surgical mastoiditis, the result of a thrombus directly from the respiratory tract, and developing concomitantly with the mastoid thrombi found later at operation. But of most interest here is the unusually long period of illness in those cases of acute purulent otitis media (exclusive of the cases of mastoiditis) having origin in otitis externa. The average duration of illness in these cases was nineteen days and the average duration of treatment was seventeen days.

In thirteen cases we could not state definitely the cause of the otitis media.

Realizing the difficulty of securing uncontaminated cultures in these cases and the difficulty of interpreting negative cultures, we did not attempt this procedure. We have contented ourselves thus far with attempting to correlate the type of discharge found at the onset with the gross etiological factor, the yearly incidence, the duration, and the complications and sequellæ.

TABLE II

Year	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	Totals
Sanguino-serous	5	8	5	21	4	2	6	10	5	9	8	7	90
Sanguino-purulent	6	4	6	15	12	5	10	10	11	11	7	4	101
Sero-purulent	1	....	....	4	1	1	1	3	2	1	....	1	15
Purulent	....	3	4	14	11	11	16	10	6	4	5	5	89
Muco-purulent (stringy)	....	....	2	....	....	....	1	1	....	1	....	1	6
Blebs	1	....	2	6	3	3	4	6	2	4	....	....	31
Gas	....	....	....	4	....	....	2	2	1	1	1	3	14
Hemorrhagic	1	....	5	5	2	1	2	3	1	4	2	2	28

Table II presents the number of cases of each type of discharge found at onset during each year. Because a number of cases produced discharge presenting several characteristics (e. g., blebs of the external canal, gas under pressure in the middle ear, or hemorrhage in addition to a serous or purulent discharge) the total figures here presented outnumber the total number of cases. All cases developed a purulent, and finally a mucoid discharge during the period of observation.

In order of frequency we find sanguino-purulent (101), sanguino-serous (90), and purulent (89). In twenty-eight cases a purely hemorrhagic discharge was seen.

TABLE III

Year	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	Totals
Surgical Mastoiditis	....	1	1	....	2	....	....	....	....	....	4
Non-surg. Mastoiditis	2	3	1	1	2	....	3	1	4	1	18
Hemorrhage	2	....	1	....	....	....	....	....	....	....	3
Ulceration Tympanum and Tympanic Membrane	2	....	1	....	1	....	....	....	....	....	4
Petrositis	....	....	....	1	....	....	....	....	....	....	1
Permanent Perforations	....	....	....	....	1	....	1	....	....	....	2

Table III discloses the yearly incidence of complications and sequellæ.

There was one case of petrositis which resulted fatally. Autopsy disclosed a mastoid that was normal except for a scant terminal exudate, and that the route to the apex was via a chain of peritubal cells.

There were four cases of extensive ulceration and necrosis of the tympanic membrane and middle ear mucosa, and there were three cases of severe hemorrhage.

Two cases were dismissed with permanent perforations in spite of all attempts to produce closure. Here the infective process in the tympanum and paratympanum had been arrested and healing had otherwise occurred.

There were only four cases of surgical mastoiditis, and there were eighteen cases of non-surgical mastoiditis.

TABLE IV

Year	Etiology	Discharge	Type	Hyperplasia Sub-Mucosa
1929	Scarlet fever	Gas—Sanguino-purulent	Type II—Thromb.	No
1930	Influenza	Sanguino-purulent	Type II—Thromb.	No
1932	Otitis Externa	Sanguino-purulent	Type II—Thromb.	No
1932	Influenza	Purulent	Type II—Hemorr.	No

Table IV concerns the cases of surgical mastoiditis.

The astonishingly low incidence of 1.3 per cent is to us a source of deep satisfaction. The lowest comparable figures to which we have access show an incidence varying from 8 per cent to 10 per cent. We find that all the cases of surgical mastoiditis followed the more severe upper respiratory infections, except the one case following otitis externa which has been discussed; that none showed a hyperplastic submucosa at the onset, and that all followed a type II otitis media, one being of the true hemorrhagic type and three being of the thrombotic type.

TABLE V

Year	Etiology	Discharge	Hyperplasia Sub-Mucosa
1928	Cold	Purulent	No
1928	Cold	Sanguino-purulent	Yes
1929	Tonsillitis	Hemorrhagic	No
1929	Flu.-Sinusitis	Purulent	Yes
1929	Cold-Tonsillitis	Sanguino-purulent	Yes
1930	Flu.-Sinusitis	Blebs. Sang.-purulent	No
1931	Flu.	Blebs. Sang.-purulent	No
1932	Flu.	Sanguino-purulent	Yes
1932	Cold	Purulent	Yes
1934	Cold	Purulent	No
1934	Sinusitis	Blebs. Hemorrhagic	Yes
1934	Flu.	Sanguino-serous	Yes
1935	Flu.	Sanguino-purulent	Yes
1936	Flu.	Purulent	No
1936	Flu.	Sanguino-serous	No
1936	Flu.	Sanguino-purulent	No
1936	Cold	Purulent	Yes
1937	Cold	Sanguino-purulent	No

Table V concerns the cases of non-surgical mastoiditis.

There were eighteen such cases; an incidence of 6 per cent. In this classification we placed those cases that appeared to have mastoiditis, but which cleared under expectant treatment. The following group of criteria on which this diagnosis was based were present: pain, tenderness, and definite edema of the mastoid; elevation of temperature beyond the usual time and above the usual limits with no other cause present; beginning sagging of the posterior-superior canal wall; increased signs of general physical involvement, and usually a clouding of the antrum and mastoid cells on X-ray beyond the amount of clouding usually found in early acute purulent otitis media.

Here we find the severer types of upper respiratory infections preceding the otitis media. In nine cases (50 per cent) there was a hyperplastic submucosa. These nine cases also represented 50 per cent of the total of eighteen cases of hyperplasia of the submucosa found in the entire series of three hundred cases. This finding must have etiological importance. It would indicate that hyperplasia of the submucosa, probably because of the increase of inter-cellular spaces, predisposes to type III mastoiditis but not to type II.

Of further significance may be the fact that the combined incidence of surgical and non-surgical mastoiditis (7.3 per cent) closely approaches the usually quoted figures of 8 per cent to 10 per cent for the incidence of surgical mastoiditis.

SUMMARY AND CONCLUSIONS

1. Certain anatomical arrangements of the tympanum and paratympanum, and certain pathological processes connected therewith are described and discussed from an apparently original viewpoint.

2. A method of treatment based thereon has been evolved from older known methods.

3. From the results obtained in extended clinical experience therewith we feel

a. That the period of disability has been shortened considerably.

b. That the number of cases of permanent disability has been reduced sharply.

c. That no case (or at worst, very few cases) of surgical mastoiditis of the so-called coalescent type ever should be allowed to develop from acute purulent otitis media.

d. That the only cases of inevitable surgical mastoiditis are those that are a part of type II acute otitis media.

514 Medical Arts Bldg.

REFERENCES

1. Sellers, L. M.: A Preliminary Report of the Results of Suction Treatment in 150 Consecutive Cases of Acute Purulent Otitis Media. Texas State J. Med., 28:351-354 (Sept.), 1932.

2. Fridenberg, Percy: Aspiration of the Tympanic Cavity in Otitis Media. Annals of Otology, Rhinology and Laryngology (Sept.), 1906.

3. Fridenberg, Percy: Aspiration of the Tympanic Cavity After Paracentesis; a Valuable Aid in the Treatment of Otitis Media. Med. Rec. (March 3), 1906.

4. Fridenberg, Percy: Simple Apparatus for Aspiration and Evacuation of the Tympanic Cavity After Paracentesis. Med. Rec. (March 7), 1908.

5. Wagers, Arthur J.: The Use of Suction in Otolaryngology; Technique of Application. Therap. Gaz., 45:80 (Feb. 15), 1931.

6. Politzer, Adam (and Ballin, M. J.): Diseases of the Ear; Lea and Febiger, 1926; pp. 365 and 367.

7. Linck, A.: Report of Abstract, Arch. Ohr., Hals., Nasenheilk., 129:181, 1931, by Keen, J. A.; J. Laryng., 46:855 (Dec.), 1931.

8. Sellers, L. M.: The Rationale of Treatment in Otitis Media. Read before the Texas Panhandle District Medical Society, Amarillo, Texas, April 16, 1935.

9. Sellers, L. M.: Otitis Media; A Problem in Double Drainage. Read before the Texas State Ophthalmological and Otolaryngological Society at Houston, Texas, December 10, 1935.

10. Hadjopoulos, L. G., and Bell, J. W.: Direct Versus Intermediate Pathways in Infections of the Mastoid. Arch. Otolar., 25:6 (June), 1937.

11. Wittmaack, Karl: Die Entzundlichen Erkrankungsprozesse des Gehororganes, Handbuch der Speziellen Pathologischen Anatomie un Histologie (Henke and Lubarsch), 12:126.

12. Kopetzky, S. J.: Otologic Surgery. Paul B. Hoeber, 1929, p. 4.

13. Greenfield, Samuel D.: Thrombophlebitis of the Lateral Sinus. Arch. Otol., 25:661 (June), 1937.

14. Woods, R. R.: Painful and Dangerous Diseases of the Ear. Oxford University Press, 1936, p. 8.

15. Tremble, G. E.: The Clinical Importance of the Mastoid Antrum. Arch. Otol., 15:575 (April), 1932.

16. Ballance, Charles: Surgery of the Temporal Bone. MacMillan Co., 1919, Vol. 1, plate XXXI, fig. 5.

17. Kerrison, Philip D.: Diseases of the Ear. J. B. Lippincott Co., 1921, p. 169.

Clinical Notes

LXXXVII

THE USE OF PRONTOSIL AND SULFANILAMIDE IN THE TREATMENT OF OTOGENIC MENINGITIS: REPORT OF EIGHT CASES*

ROBERT B. LEWY, M.D.

CHICAGO

The therapeutic value of prontosil and sulfanilamide in the treatment of otogenic meningitis is rapidly becoming well established. The reports of their use in the treatment of streptococcic meningitis by Weinberg and Mellon[1] prove their efficacy in contrast to the infrequency of recovery demonstrated in Gray's series.[2] The broadening horizon brings with it new problems as to the technique of handling meningitis cases, the control of the unpleasant and perhaps dangerous side reactions of these drugs, and the possibility of reducing the amount of surgery previously considered necessary in treating these conditions.

Eight cases are herewith presented of established meningitis treated with these drugs; five of these demonstrated beta streptococcus hemolyticus on culture of the spinal fluid or at autopsy. Five of the eight and three of the five beta streptococcus hemolyticus cases are now living and well.

REPORT OF CASES

CASE 1.—J. H., age 4, admitted March 8, 1937, discharged April 5, 1937. The child was in excellent health until one week prior to admission when he developed a cold. After a period of time this seemed to settle in his neck and the neck became stiff. The temperature at the onset was up to 102 and has remained at that level. Stiff neck and pain in the neck set in three days prior to entrance. The child was admitted to the contagious hospital as a suspect epidemic meningitis but examination did not prove this diagnosis. A discharging right ear was found and the child was transferred to the ear, nose and throat department.

*From the Services of Dr. Louis T. Curry, Dr. Thomas C. Galloway, Dr. Alfred Lewy, Dr. Irving Muskat, Dr. Samuel J. Pearlman. The Department of Otolaryngology, Cook County Hospital.

Physical examination revealed a well developed and fairly nourished white male child acutely ill. Temperature 102°, pulse 124, respiration 24.

Right ear: There was a slight mucoid discharge. There was a perforation in the central portion.

Left ear: The drum was injected and bulging.

Neck: Marked rigidity.

Kernig's sign positive.

Brudzinski's sign positive.

Spinal puncture: Clear fluid, Pandy ++++, cells 20, mostly polys.

Laboratory: Urine negative; normal differential blood count.

Operation: Right simple mastoidectomy. The dura of the middle and posterior fossa was exposed. The dura of both these regions was normal but there was a perisinus abscess.

Postoperative Course: The child progressed well for the first five days, running only a low grade temperature. However, on the fifth day he developed rather marked meningeal symptoms again. Spinal puncture done at this time revealed 85 cells. These symptoms subsided the following day and two days later the cell count was down to four. The child then staged an uneventful recovery except that it took him about two weeks to regain his ability to walk.

Comment: This patient had only 5 cc. of Prontosil. The meningitis was well localized. It is highly probable that the surgery alone would have saved the patient.

CASE 2.—E. R., age 9, admitted March 8, 1937, discharged March 30, 1937. This nine-year-old white child was admitted to the ear, nose and throat ward of Cook County Hospital on March 8, 1937. Two years prior to admission she had a discharging ear for a short time, it is not known which ear. This subsided spontaneously and she had no trouble until fourteen days before admission. At this time she had a head cold. Nine days before admission the right ear began to drain profusely. After six days this subsided somewhat. For five days before entrance there had been a marked deafness in the left ear. There was no history of nausea or dizziness but the child vomited three times preceding paracentesis of the left ear. On March 6, 1937, she developed a severe headache and a stiff neck. This persisted and was accompanied by a temperature of 104.5° m.

Physical Examination revealed a well developed and well nourished white child acutely ill. Temperature 104.4°, pulse 124, respiration 24.

Right Ear: Drum red, no landmarks visible. Spoken voice heard at two feet. C 64 not heard. C 56, 2048 were both shortened. Partial peripheral left facial paralysis.

Left Ear: Totally deaf.

Caloric Tests: No alteration of the existing nystagmus with either ear.

Weber Test: Heard on the right side.

Rinné: Negative both sides.

Schwabach: Prolonged.

Kernig: +-+-+.

Brudzinski: +-+-+.

Spontaneous rotary nystagmus to the right.

Spinal Fluid: Cloudy. Increased pressure. Pandy positive. Few gram + strep. on smear. 1000 cells mostly polymorphial nuclear leucocytes.

Pathology at Operation: Right side. The periantral bone was softened as was the dural plate. The dura and lateral sinus appeared normal.

Left side. The dura of the middle fossa was slightly reddened. On attempting to open the labyrinth there was a twitching of the face and a left facial was present after the operation.

Postoperative Course: The child was placed on intensive therapy with prontosil and prontylin. She was given 5 cc. of the former every four hours intramuscularly for the first four days and grains x of the tablets by mouth every four hours. Meanwhile a series of spinal punctures were made. On March 8, March 9 and March 10 the cultures were positive for strep. hemolyticus. The last report showed the organism less hemolytic. Following this no organisms could be cultured. During this period she also received two blood transfusions.

In five days the temperature dropped to normal and she was discharged on March 30, 1937. Since this time the left facial has disappeared and hearing in the left ear is returned so that the loud spoken voice can be heard, using the noise apparatus in the opposite ear.

Comment: There were minimal changes found in the dura and the mastoid bone in this case. One seriously questions whether the patient would not have recovered if she had had no surgery, but only the prontosil, sulfanilamide, blood transfusions and other supportive treatment.

CASE 3.—J. L., age 50, admitted February 12, 1937, discharged March 13, 1937. This fifty-year-old white female was first admitted to the ear, nose and throat ward of Cook County Hospital on February 12, 1937. At this time she was complaining of moderate bilateral aural discharge for several years. For two weeks the left ear had been discharging profusely and she had marked post auricular pain. For three days prior to entrance she had a marked cough with profuse expectoration. Chest examination disclosed a pneumonia and she was sent to a medical ward. After seven days the chest findings subsided and the discharge from the left ear became more profuse. She developed a concomitant sinusitis. The patient began to run a temperature as high as 103 and it was felt that a radical mastoid was indicated.

Physical Examination: Left ear, profuse very foul discharge. Anterior inferior perforation and one polyp in the ear canal.

Right ear membrana tympani almost all missing, otherwise normal.

Operation was performed on the left ear. Numerous granulations were found in the mastoid antrum and at the mastoid tip.

Postoperative Course: Despite the operation the patient continued to run a septic temperature. Spinal fluid was examined and this was negative. Three successive blood cultures were positive for hemolytic streptococci. The patient was put on prontosil and prontylin and given three blood transfusions. She improved steadily but had a severe reaction to each transfusion with a marked rise in temperature. On March 13, 1937, she was discharged apparently cured. On March 19, 1937, she reappeared at the clinic appearing very pale and acutely ill. Because of the marked pallor and palpable spleen and absence of ear symptoms she was sent to medicine as a subacute bacterial endocarditis. She developed a severe headache which persisted. Spinal puncture done March 20, 1937, was negative. The following day, however, she had a stiff neck, Kernig's +-++ and Brudzinski +++. Spinal puncture at this time revealed cloudy fluid, 2500 cells, gram+ diplococci and increased pressure. The Pandy tests were positive. Culture from the spinal fluid revealed streptococcus hemolyticus.

The patient was reoperated on and the dura of the middle and posterior fossa widely exposed. There was a slight injection of the dura of the middle fossa. The lateral sinus was compressible, patent and slightly gray at the upper end. Since she was conscious and rational she was put on sulfanilamide by mouth. Spinal fluid cultures March 25 and March 27 were positive for strep. hemolyticus, Spinal fluid cultures and subculture were negative on March 29, March 31, April 1 and April 2. The patient rapidly improved and was discharged as cured.

Laboratory: W. B. C. 10,500, 14,500. Urine negative. Wassermann negative.

Comment: There were minimal changes found in the dura and the mastoid bone in this case. One seriously questions whether the patient would not have recovered if she had had no surgery, but only the prontosyl, sulfanilamide, blood transfusions, and other supportive treatment.

CASE 4.—J. A., age 49, admitted February 4, 1937, died April 6, 1937. This patient's history dates back to February, 1935, when she entered the E. N. T clinic. At this time she had an acute otitis media on the right side. Paracentesis was performed and the ear cleared up in a short time. On August 1, 1935, she had a left otitis media and the right ear discharged at the same time. On August 14 both ears stopped draining and she felt quite well until February, when she developed an acute upper respiratory infection. Shortly following this both ears started draining again. This was associated with bilateral mastoid tenderness most marked on the left side. X-ray of the mastoid at this time showed a moderate degree of cloudiness most marked in the left mastoid. The pain and tenderness increased over the left mastoid. Physical findings at the time of admission revealed a dry right ear with some scarring of the drum. The left ear was discharging profusely. There was an anterior perforation of the left ear drum, marked discharge and marked mastoid tenderness mostly over the tip and the antrum. The Weber test lateralized to the left. The whispered voice was reduced to eight feet. Caloric tests produced a normal response in both ears. Left mastoidectomy was performed and the patient recovered uneventfully with a dry ear at the end of eight days. Although the ear was apparently cured she continued to complain of slight headache on the right side of the head. On March 31, 1937, she returned to the clinic with a slight drainage at the lower end of the mastoid wound and a full blown erysipelas on the left side of face and left ear. She was sent to the contagious hospital where the erysipelas was treated with ultraviolet

light. Here the patient suddenly became comatose, developed twitchings of the hands and developed a marked stiff neck.

Physical Examination on re-entrance to the E. N. T. department showed a well developed and well nourished colored female in coma and acutely ill. Temperature 105°, pulse 135, respiration 40.

Left Ear: Old mastoid scar with slight draining area at the lower end of the wound. Fading erysipelas on the left side of the face.

Kernig's: +++.

Brudzinski: +++.

Stiff Neck: Very marked.

Spinal Fluid: Cloudy. Under increased pressure slight xanthochromic tinge.

Laboratory: Hemoglobin, 85 per cent; white blood count, 10,150.

Operation: Reopening through the old mastoid wound. Part of the facial bridge was cut down. The dura of the posterior and middle fossa was widely exposed. There were granulations over the dura of the middle fossa in the area of the tegmen antri. The lateral sinus and dura of the posterior fossa were normal.

Postoperative Course: The patient was given prontosil 5 cc. every four hours but remained unconscious and died twenty hours after admission and operation.

Postmortem: Acute suppurative basilar leptomeningitis (Streptococcus hemolyticus).

Suppurative otitis media of the left side.

Benign nephrosclerosis.

Hydrothorax of the left side.

Comment: The autopsy revealed a far advanced meningitis. It is obvious in retrospect that nothing could save this patient.

CASE 5.—G. O., age 5 months, admitted May 17, 1937, died June 16, 1937. Only a very limited history was available in this case as the only informant did not speak English. It was ascertained that the child had some purulent discharge from both eyes and a purulent discharge from the right ear of two months' duration. Two weeks prior to entrance he had chickenpox. Eleven days after admission to the hospital he suddenly developed twitching of the right arm. At the same time there was a marked lethargy and the temperature rose to 102.6 degrees axillary.

Physical examination revealed a fairly developed and nourished white male infant acutely ill. Temperature 102.6°, pulse not obtained, respiration 30-38.

Right Ear: There was a moderate amount of foul smelling purulent discharge. Hearing was present. Drum pale and bulging, no perforation seen. No mastoid swelling or tenderness.

Left Ear: Essentially normal.

Stiff Neck.

Brudzinski sign positive.

Spinal fluid increased pressure. Fluid cloudy. 1575 cells mostly polymorphs. Chains and pairs of Gram positive diplococci on the direct smear.

Laboratory: Successive cultures of the spinal fluid showed

1 streptococcus hemolyticus a and Viridans.
2 streptococcus a hemolytic.
3 streptococcus a hemolytic.
4 streptococcus a hemolytic.
5 streptococcus anhemolyticus.
6 streptococcus anhemolyticus (June 13, 1937).

Urine Albumin ++ Few cells and granular casts.

W. B. C. 15,500. Normal differential.

Spinal fluid sugar

1 52 mgm. per 100 cc. (May 29, 1937).
2 32 mgm. per 100 cc. (June 3, 1937).
3 0 mgm. per 100 cc. (June 7, 1937).

Operation: Mastoidectomy performed May 29, 1937, with exposure of the dura of the middle and posterior fossa. The mastoid was free of pus or granulations. The mucosa of the middle ear appeared somewhat thickened. The dura of the posterior and middle fossa was white and unchanged in color but felt slightly tense.

Postoperative Course: The day following operation the temperature was 103 degrees ax. but the twitchings had stopped. Spinal fluid at this time showed 1800 cells. He was given 5 cc. of prontosil intramuscularly twice, starting immediately after the operation. At the same time he was given sulfanilamide gr. 1¼ every four hours. The following day the temperature was 100°, the child was eating well and seemed greatly improved. By June 1 the temperature dropped to 99 degrees ax. The spinal fluid was clear and there were 280 cells. By

June 6 the child became markedly jaundiced. Because of this the dose of sulfanilamide was reduced by one-half. The next day the temperature rose to 103° and the child developed symptoms of pneumonia, which was proven by x-ray. By June 10 the child was, it seemed, almost terminal. The temperature went to 107°. It again became very rigid. The dose of sulfanilamide was increased to that which it received originally. After 24 hours the temperature dropped to 94° but rapidly climbed again. The child lingered until June 16, 1937, and finally died one month after admission and seventeen days after the onset of meningitis.

Comment: Beta streptococcus hemolyticus was found only as a contaminant in the cultures on this patient. Failure may have been due to the lack of specificity of the drug for the alpha streptococcus hemolyticus. Nevertheless, the clinical impression is that these drugs controlled the meningitis for a short while and definitely prolonged the life of the infant. There remains a distinct possibility that if the dosage of the drug had not been reduced when the complications set in the patient might have been saved. This is borne out by the fact that there was a definite temporary improvement when the dose was again increased with the patient apparently moribund and temperature of 107°.

Case 6.—A. A., age 7 years, admitted March 7, 1937, died March 17, 1937. This patient was in good health until three weeks prior to entrance into the hospital. At this time the right ear began to drain spontaneously, but she felt quite well. She continued to feel well until three days prior to admission, when she developed a severe pain in the right ear. This pain in the ear continued unabated until one day before entrance, at which time she developed a high fever and some stiffness of the neck.

Physical examination revealed a well developed and fairly nourished white female child acutely ill. Temperature 104 , pulse 144, respiration 30.

Right Ear: Hearing diminished but present profuse mucopurulent discharge. Drum not seen.

Left Ear: Essentially normal.

Kernig's: ++.

Brudzinski: ++.

Marked stiff neck.

Spinal Fluid: Cloudy, increased pressure, 1600 cells, mostly lymphocytes. Streptococci and diplococci seen on smear.

Laboratory: Spinal fluid culture revealed streptococcus hemolyticus.

Urine: Negative.

Operation: Simple mastoidectomy with exposure of the dura of the middle and posterior fossae. Dura over the temporal lobe very red, especially over the base. Lateral sinus a little grayer than normal. Sclerotic mastoid with slight softening around the mastoid antrum.

Postoperative Course: The patient was given a total of 30 cc. of prontosil and 30 gr. of prontylin in the first three days postoperatively. She was also given two blood transfusions and adequate subcutaneous and intravenous fluids and glucose. The day after the operation she was conscious and clear minded, but her general condition remained poor. Her temperature never became lower than 101°. After the first three postoperative days the spinal fluid cell count became progressively higher and her temperature began to rise. Two days before her demise she slipped into coma. She died on March 17, 1937, ten days after admission and operation and four weeks after the onset of the discharge from the ear.

Postmortem: Suppurative leptomeningitis (hemolytic streptococcus).

Hemorrhagic bronchopneumonia of the right upper and lower pulmonary lobes.

Acute emphysema of the lungs.

Parenchymatous degeneration of the liver, myocardium and kidneys.

Subinvolution of the thymus.

Comment: Only a limited amount of drug was available for the treatment of this patient. Also note that this patient had a very red dura. It is felt that these drugs prolonged the patient's life.

CASE 7.—E. B., age 11, admitted May 26, 1937. About one week prior to entrance this 11-year-old white male child had a slight cold. This was followed by pain in the left ear in turn followed by profuse discharge for four to five days. He had a headache almost from the onset of his symptoms and vomiting, fever and rigidity of the neck for three to four days. Walking was increasingly difficult because of marked dizziness.

Physical examination revealed a well developed and well nourished white male child acutely ill. Temperature 102.8°, pulse 110, blood pressure 160:110.

Left ear revealed a central perforation from which came a thick foul-smelling discharge.

Marked spontaneous nystagmus both horizontal and vertical, most marked to the right.

Hearing present in both ears, slightly reduced in the left.

Slight tenderness over the left mastoid tip.

Kernig's: +++.

Brudzinski's: +++.

Marked stiff neck.

Spinal puncture: Fluid cloudy. Cell count 3,200. Gram + diplococci on smear.

Laboratory: Streptococcus hemolyticus cultured from spinal fluid on May 26, 1937 and May 27, 1937. Also cultured from ear. Additional later cultures revealed no growth.

Spinal fluid sugar 24 mgm. Chlorides 580 mgm.

W. B. C., 36,150, May 26; 16,150, May 28.

Urine negative.

Operation: Coalescent area with cavity in Trautman's triangle of the left mastoid. Many granulations at the mastoid tip. Dura of the posterior fossa, middle fossa and lateral sinus normal.

Postoperative Course: The child was placed on intensive therapy with prontosil and sulfanilamide. He received 5. cc. of prontosil every six hours intramuscularly for the first three days. This was accompanied by 15 gr. sulfanilamide every four hours for the first three days. At the end of this period the child was slightly cyanotic and the prontosil was stopped and the dose of sulfanilamide reduced. The cyanosis promptly disappeared. Spinal fluid counts dropped, the temperature gradually came down to normal on the tenth postoperative day. The child was discharged on June 24, 1937, twenty-eight days after admission.

Comment: The lack of any significant change in the dura and the minimal amount of destruction in the mastoid bone again raise the question of the necessity of such extensive surgery.

CASE 8.—J. K., age 9, admitted May 26, 1937. On approximately May 10, 1937, this child developed a bilateral otitis media for which paracentesis was performed. At this time he was hospitalized in another institution and kept there for ten days. He was

TABLE I

Initials and Age	History	Prontosil and Sulfanilamide	Transfusions	Operation
J. H. 4	Head cold, right aural discharge one week. Fever 102 from onset.	5 cc. of prontosil.	1 350 cc.	Right mastoidectomy. Exposure of dura of middle and posterior fossae.
E. R. 9	Aural discharge few days. Deafness left ear three days.	65 cc. prontosil. 80 gr. sulfanilamide.	3 500 cc.	Right mastoidectomy. Left radical. Exposure of dura of middle and posterior fossae.
J. L. 50	Aural discharge both ears several years. Pneumonia, radical mastoid, later meningitis.	120 cc. prontosil. 120 gr. sulfanilamide.	4 3 reactions	Left mastoid reoperated with exposure of dura of middle and posterior fossae.
J. A. 49	Ancient acute otitis media bilateralis. Right mastoidectomy. Fistula, erysipelas. Sudden onset of meningitis.	20 cc. prontosil.	—	Reoperated mastoid with exposure of dura of posterior and middle fossae.
G. O. 5 mos.	Discharging right ear two months—Varicella. Sudden onset twitching and lethargy.	20 cc. prontosil. 60 gr. sulfanilamide.	2— 250 cc.	Right antrotomy. Exposure of dura of posterior and middle fossae.
A. A. 7	Spontaneous discharge right ear three weeks. High fever, stiff neck 24 hours.	30 cc. prontosil. 30 gr. prontolyn.	2 500 cc.	Simple mastoid. Exposure of dura of posterior and middle fossae.
E. B. 11	Acute rhinitis 1 week. Draining ear 1 week. Fever, headache 4 days.	60 cc. prontosil. 1260 gr. sulfanilamide.	None	Simple mastoid. Exposure of dura as above.
J. K. 9	Previous bilateral otitis media 2½ weeks. This had stopped 5 days. Followed by meningitis.	10 cc. prontosil. 1460 gr. sulfanilamide.	1 500 cc.	Bilateral simple mastoid. Exposure of dura of posterior and middle fossa.

TABLE I—(Continued)

Pathology	Smear	Spinal Fluid		Sugar	Mastoid	Outcome
		Culture	Cell Count			
Perisinus abscess.	No organisms	No growth	20 polys. 4 on P. O. II.	95 mgm.	Staph. aureus	Cured.
Questionable injection of dura on left side.	Gram pos. streptococci	Strep. hemolyt. b. (3)	5780 500 200 Polys.	——	——	Cured.
Slight grayness upper lateral sinus.	No organisms	Strep. hemolyt. b.	2800 mostly polys.	——	——	Cured.
Granulations over the dura of the middle fossa.	——	——	Cloudy. Increased pressure. Pandy pos.	——	——	Fatal.
Dura normal color. Felt slightly tense.	Gram pos. diplococci	Strep. hemolyt. a. and strep. viridans	1180 870 1650 720 Polys.	52 mgm. 32 mgm. 0 mgm.	——	Fatal.
Dura very red over the middle fossa.	Gram pos. streptoc.	Strep. hemolyt. b.	1600 6300 Polys.	——	——	Fatal.
Dura normal. Cavity in Trautman's triangle.	Gram pos. diplococci	Strep. hemolyt. b.	3200 5600 Polys.	24 mgm.	Strep. hemolyt. a.	Cured.
Normal dura and mastoids both sides.	Gram pos. diplococci	No growth.	7150 1200 45	56 mgm. 76 mgm.	No growth.	Cured.

discharged from this hospital with both ears apparently dry on May 20, 1937. On May 24, 1937, the child complained of severe generalized headache and had a noticeable stiff neck. On May 25 the child had very forceful vomiting. On May 26 the child was delirious part of the time, the neck was very stiff and the head held back.

Physical examination revealed a well developed and well nourished colored male child acutely ill. Temperature 104.5 degrees R, pulse 100, respiration 22.

Right Ear: Slight thickening of the drum. Landmarks visible. Whispered voice heard at eight feet. Canals intact, Rinné negative.

Left Ear: Slight injection of Shrapnell's membrane. Whispered voice heard at eight feet. Rinné negative.

Weber test did not lateralize.

Kernig's: +-++.

Brudzinski: +-++.

Marked stiff neck.

Spinal puncture: Fluid cloudy. Cells 7,150. Pressure increased. Pandy test positive. Gram + diplococci seen on one smear. Cultures negative.

Laboratory: W. B. C., 28,120; after three days, 12,000.

Urine negative.

Spinal fluid sugar 56 mgm. Chlorides 780.

Operation: Performed May 27, 1937. Bilateral mastoidectomy was done with exposure of the dura of the posterior and middle fossæ of both sides. The dura was normal. There were a few granulations in the body of each mastoid process.

Postoperative Course: The child was placed on intensive therapy with prontosil and sulfanilamide. He received 5 cc. of prontosil every six hours intramuscularly. With this he received 15 gr. sulfanilamide every four hours for the first three days. This was reduced to 10 gr., and at the end of nine days to 5 gr. On the first day postoperative his maximum temperature was 101 degrees R. He had stopped vomiting and was quite rational. By the seventh day his temperature was normal. The cell count in the spinal fluid dropped to 45 by postoperative II. Three weeks later he again developed a fever and meningeal symptoms. He was placed on sulfanilamide again, spinal fluid cell count 840. After several days the temperature again returned to normal and the child was discharged six weeks after the onset of his meningeal symptoms.

Comment: Here again the lack of changes in the dura and the mastoid bone raise the question of whether any surgery was necessary.

TECHNIQUE OF HANDLING CASES

1. All cases which had discharging ears and could not be established as epidemic meningitis were treated as otogenic.

2. These cases were considered surgical emergencies and operated as soon as possible.

3. Blood transfusions were given liberally in all but one case—this patient had a hypertension.

4. Comatose and vomiting patients were given an intensive course of intramuscular prontosil immediately; rational patients were given prontosil for two days, combined with sulfanilamide orally. (One patient received only oral sulfanilamide and recovered.

5. Daily spinal punctures were performed wherever symptoms of marked meningeal irritation persisted.

6. Intravenous glucose 5 per cent and other supportive measures were given as indicated.

COMMENT

Although the mortality in this series is somewhat higher than that of the other recent reports, [1 3 4] it seems obvious that prontosil and sulfanilamide were largely responsible for the recoveries.

Of the six cases that demonstrated organisms on culture of the spinal fluid (one was a postmortem culture), three were fatal. Of the three fatal cases, two were caused by streptococcus hemolyticus. One of the patients showed profound changes in the dura and was obviously too near her demise to be saved; one may have died because of the lack of specificity of the drug for the alpha type, although this and the third fatal case both seemed to have been aided by the drugs, and lived longer than the average meningitis patient. One of the successful cases demonstrated organisms on smear but not on culture. The others showed no organisms at any time. As indicated, five of the patients lived.

This group may be contrasted with past results in which even in the more favorable cases, i. e., no organisms seen on either smear or culture but definite meningeal signs and symptoms, the patients almost always died.

One distinct new problem now confronts the otologist. In otogenic meningitis with an acute ear history and no mastoid swelling or tenderness should operation be performed? Weinberg and Mellon[1] and Anderson[4] both report successful cases unoperated except for paracentesis, with recovery. It seems probable in retrospect that three cases in this series would have recovered without operation.

COMPLICATIONS

One of the cases in this series developed a moderate cyanosis; the dose of the drug was halved, the cyanosis disappeared and the patient went on to recovery. In another case a marked icterus developed. This may or may not have been a complication of the use of the drugs. When the dose of the drug was reduced the patient got worse promptly, but the icterus did not improve.

Some very recent experiments indicate that equivalent doses of sodium bicarbonate administered with the drug may avoid these complications.

CONCLUSIONS

Eight cases of otogenic meningitis, five of which were caused by streptococcus hemolyticus are here presented:

1. The excellent results obtained add further weight to the already established value of prontosil and sulfanilamide in the treatment of this condition.

2. The elimination of a large amount of the surgery now done in otogenic meningitis may be in the offing, but it would still seem advisable to operate all cases of otogenic meningitis until our diagnostic skill is improved. The necessity seems greater with chronic than acute ears.

3. The urgency of the use of prontosil and sulfanilamide in the earlier, more fulminating stages of meningitis seems greater than the necessity of stopping their use because of complications. In the latter case it may be worth while to reduce the dosage.

4. Despite the improvement in the mortality in otogenic meningitis with these agents, they must be considered only an adjuvant in the already established treatment.

5. It seems advisable to administer prontosil and sulfanilamide as empirical treatment of all otogenic meningitis regardless of the absence of positive spinal fluid cultures.

25 East Washington Street.

REFERENCES

1. Weinberg, M. H., Mellon, R. R.: Two cases of Streptococcic Meningitis Treated Successfully with Prontosil and Sulfanilamide.

2. Gray, H. J.: Streptococcic Meningitis; J. A. M. A., 105, p. 92 (July), 1935.

3. Schwenkert, Clason, et al: Johns Hopkins Hospital Bull., 60:297, April, 1937.

4. Anderson, E. D.: Streptococcic Meningitis. J. A. M. A., p. 1591, May 8, 1937.

LXXXVIII

SPONTANEOUS AMPUTATION OF THE NOSE DUE TO DIABETIC GANGRENE WITH CASE REPORT*

THOMAS B. WOOD, M.D.

BROOKLYN

This report is to call attention to the fact that diabetic gangrene of the nose, although of rare occurrence, is an established entity, in which the total loss of the nose, a terrible disfiguration, may result. The author, as yet, has not been able to find a case of spontaneous amputation of the nose, in the literature.

Bowers[1] of Los Angeles in 1924 reported three cases of "Gangrene of the Nose Complicating Diabetes" in which he quotes Sturges (1892) and Buerger[2] in the general discussion of gangrene. His cases were all in children, in two of whom the nasal septum was lost and in the other there was involvement of the left side of the nose, the left cheek and the left upper lip. He failed to find any previous cases in the literature.

Connell[3] of Kansas City, later in the same year, reported a case of "Diabetic Gangrene of the Nose" in an adult male with perforation of the nasal septum and hard palate into the right maxillary antrum. He also failed to find previous mention of this condition in the literature.

Ardeshir,[4] England, in 1926, reported a case of "Gangrene of the Nose Due to Diabetes Mellitus" in an Indian female child which resulted in a loss of the left alar cartilage. His search of the literature discovered only the article of Bowers' written two years previously.

In 1929, Bulger[5] reported a case of gangrene of the orbit and nares in diabetes mellitus in a young married woman with involvement of the left side of the nose and inner aspect of the orbit of the left eye, which resulted in death from coma.

This totals only six cases that the author can find in his search of the literature. The mortality in these six cases, under the best treatment available at the time, was 50%.† It must be borne in

*From the Department of Otolaryngology of the Coney Island Hospital.

†Of these, two had the benefit of insulin therapy.

mind that three of these cases were treated before the advent of insulin. In no case was there a total loss of the external nose.

REPORT OF A CASE

CASE 1.—M. C., a white female, of about 45 years of age, was admitted by ambulance on the afternoon of June 20, 1932, in a state of deep coma of three hours' duration. Her breathing was stertorous, face flushed, nose swollen, extending to the face, with no definite line of demarcation to the swelling. Her breath had a distinct acetone odor. Heart and lungs revealed no pathology and there was no edema of the legs or sacrum. Blood pressure was 120/90; pulse regular, with good quality; knee jerks and deep reflexes were diminished but present. Immediate catheterization produced approximately 600 cc. of clear urine which showed four-plus sugar and four-plus acetone on qualitative analysis.

The history, obtained from the mother, was to the effect that two weeks previous to admission patient fainted and fell against a chair in the home, striking on her nose and causing a bruise to that member. The nose had been getting worse until just before admission when she fainted again and could not be aroused. There was no previous history of syphilis or diabetes. She had always been a very healthy woman.

The patient was put to bed in the ward with the provisional diagnosis of diabetes and erysipelas of the nose. At 7:00 p. m., still in deep coma, approximately twenty ounces of urine was removed by catheter, which also showed four-plus sugar and four-plus acetone. Fifty units of insulin was given and as the patient appeared dehydrated, a clysis of 1000 cc. of saline was instituted. At 10:00 p.m. she was given intravenous glucose 10% in 250 cc. of saline with fifty units of insulin. At this time the patient reacted for a few minutes asking for water which was given and then relapsed back into coma. At 12:00 midnight, 2:00 a. m. and 4:00 a. m., respectively, she was catheterized for urinalysis and given fifty units of insulin. At 6:00 a. m., June 21, the patient was conscious and asking for water, which was taken freely. At 8:00 a. m. a blood chemistry was ordered and standing orders for insulin, units x q.4.h., and catheterization q.4.h. were given. At 10:00 a. m. a full dose of anti-erysipelas serum was administered intramuscularly in the gluteal region. At 11:00 p. m. she was given another 1000 cc. of saline by clysis.

The patient responded so nicely to the first thirty-six hours of treatment that on June 22 she was placed on routine ward care for diabetes.

Fig. 1. M. C.: July, 1932. Sketched from life. Spontaneous amputation of nose due to diabetic gangrene of nose. Profile and front, showing line of demarcation and separation of gangrenous mass.

On June 23 erythema of the nose became more sharply outlined and extended evenly on both sides towards the cheeks. The dorsum and tip of the nose became more darkly discolored turning black at the center. The temperature varied between 99° and 100° F. The blood sugar report on specimen taken the first morning was 118 mgs./100 cc.

On June 25 the nose became more definitely gangrenous but with no definite line of demarcation, apparently the setting in of the dry stage. The erysipeloid rash continued spreading over the upper maxillary regions. The patient complained only of numbness and a feeling of congestion over the affected area. The urine showed continued excesses of both acetone and sugar. The Wassermann reaction, both antigens and the Kahn tests, were four-plus. X-rays showed no fracture of the nose.

On June 27 the urine was both acetone and sugar free, with the blood sugar down to 54 mgs./100 cc. She was then placed on a maintenance diet. The nose was entirely gangrenous.

On June 30 the blood sugar had returned to 200 mgs./100 cc.

On July 8 the gangrenous area began defining itself. The odor was characteristic and pronounced. The erysipeloid condition started clearing up; the blood sugar report showed 222 mgs./100 cc.

On July 16 the gangrenous area was dry and hard and was gradually separating. The adjacent skin was healthy.

Up to August 23, 1932, sixteen blood chemistries had been done, the blood sugar varying from 118 and 54 to 222 mgs./100 cc. The Wassermann reactions, taken at about weekly intervals, were all positive four-plus. She was kept on a strict diet and regulated insulin therapy. On this date, intensive antiluetic treatment was instituted.

One month later, on September 22, the entire gangrenous mass separated and was easily detached and removed with thumb forceps. There was no bleeding. The nasal cavity was cleaned as far back as the anterior wall of the sphenoid sinuses with cotton applicators. The entire septum was gone. The only remnants of the septum were the sphenoid crest, a small portion of the perpendicular plate of the ethmoid bone and a part of the maxillary crest. The entire external nose was gone including the nasal processes of the superior maxillæ and the nasal bones. The dense telæ of the alæ were not destroyed but were retracted inward by dense scar tissue.

The turbinates were somewhat reddened but otherwise normal. Because of the foul odor, iodoform gauze was lightly packed in the cavity.

During her stay in the hospital, 13 Wassermann tests, 128 urinalyses and 27 blood analyses were done. She was weighed at weekly intervals and showed a steady increase from 79½ lbs. on July 2, to 97 lbs. on October 21, 1932, a gain of 17½ lbs. The blood count showed R. B. C., 4,100,000, Hb. 78%; W. B. C., 7,900 with 64% polymorphonuclears and 32% lymphocytes. The temperature ranged between 99 and 100 degrees the first week and between 98.8 and 99.8 degrees the second week, with chills and uprise to 104° on July 3, and to 103.6° on July 4, after which it came down to normal and remained flat until the date of discharge.

COMMENT

On November 5, 1932, the date of discharge, the patient felt very well. She had been up and around the ward since the beginning of the antiluetic treatment and had received special instruction in the preparation of her home diet and the self-administration of insulin. Her tissues were completely healed with no remaining odor. The blood sugar was 250 mgs./100 cc. and the last Wassermann test made in 1937 was four-plus.

The absence of a nose in this patient, offered a good opportunity for the internes and staff members to study the interior of the nose without the aid of a nasal speculum. The lateral walls with the turbinates were perfectly demonstrable; the floor, posterior wall and roof of the nose were likewise in plain view; the soft palate was the most interesting to all observers, as it could be seen in action during yawning, speaking and swallowing.

At some time during her stay, the patient's true age was found to be sixty years. As she was a very co-operative patient, her request for a total reconstruction of the nose at some future date was granted.

SUMMARY

The author has been able to find only six cases of diabetic gangrene of the nose reported in the literature. The seventh reported here, presents a total, spontaneous amputation of the nose due to diabetic gangrene in a woman, sixty years of age, Wassermann fast and previously ignorant of any such disease.

878 Park Place.

BIBLIOGRAPHY

1. Bowers, Chester H. Gangrene of the Nose Complicating Diabetes. J. A. M. A., 82:17; 1325-1328 (April 26), 1924.

2. Buerger: The Pathology and Diagnosis of So-Called Diabetic Gangrene. Arch. Diag. (April), 1913.

3. Connell, Evan S.: Diabetic Gangrene of the Nose. J. Mo. Med. Assoc., 21: 277 (Aug.), 1924.

4. Ardeshir, K.: Gangrene of the Nose Due to Diabetes Mellitus. The Lancet, 1:1256 (June 26), 1926.

5. Bulger, Harold A.: Gangrene of the Orbit and Nares in Diabetes Mellitus. J. Mo. Med. Assoc., 26:304 (June), 1929.

LXXXIX

STENOSIS OF THE NASOPHARYNX: TWO CASE REPORTS

JOHN H. CHILDREY, M.D.

SAN FRANCISCO

In stenosis of the nasopharynx the soft palate and the posterior faucial pillars are adherent to the wall of the pharynx, except as a rule for a small opening immediately posterior to the uvula. Although a few cases of congenital stenosis have been reported, most of these lesions are acquired. They may be caused by infectious disease, and if so, are more often a result of syphilis. In twelve of the thirteen cases reported by Nichols[1] in 1896 the scarring resulted from syphilis. While I have observed destruction of tonsillar tissue, of the uvula or perforations of the palate and faucial pillars, as a result of syphilis, I have not observed a case of stenosis from syphilis. In the two cases which are described here, the stenosis occurred as a result of operative trauma. This accords with the finding of Figi,[2] trauma being the commonest cause in his series of eighteen cases.

The cicatricial stenosis in the cases reported herein followed operations for the removal of the tonsils and adenoids. Considering the frequency with which this operation is performed and the fact that nearly every operator attempts it, the fact that such stenosis is not a more frequent occurrence is evidence that the pharynx is able to withstand much trauma. Possibly the rarity of the condition is explained by the mobility of the palate and faucial pillars. In order to produce a stenosis the inflammatory process must be severe enough to cause fixation for a time of the soft palate, considerable fibrosis, and the epithelium must be temporarily destroyed. Probably such an explanation would account for the obstinate stenosis occurring in rhinoscleroma.

The symptoms vary with the amount and density of the scar tissue and the degree of obstruction. The voice is usually flat and lacking in resonance. If the uvula is missing and a small opening remains in the nasopharynx the voice may not be markedly affected, especially if there remains some mobility of the soft palate. These patients complain of mouth breathing, dryness of the pharynx, irritation of the larynx and discomfort in swallowing, which symptoms

are aggravated by colds. When nasal secretions accumulate in the nasopharynx, there is impairment of the sense of smell and the sinuses are liable to become diseased. Aural complications may occur as a result of disturbance in the air pressure in the nasopharynx. Although the operation for removal of tonsils and adenoids is the most frequent cause of acquired stenosis, it is not unusual to find tonsillar remnants still in the throat.

A variety of treatments have been tried in the past. The various methods, usually unsuccessful, which have been employed included incision of the scar followed by dilatation, use of the cautery, prosthetic appliances and plastic operations which have varied from the production of a cleft in the palate to the utilization of grafts or flaps of mucous membrane or skin. Following the surgical attempt at correction of the stenosis, it was often necessary to persist in digital or mechanical dilatation of the newly made opening.

Although O'Connor[3] has reported recently a case treated successfully by means of two Thiersch grafts on Stents followed by mechanical and digital dilatation, this is one of the few instances in which a plastic procedure had proved successful, and seems to be even in the hands of an expert an unnecessarily formidable undertaking.

Probably the greatest number of cures of nasopharyngeal stenosis have resulted from the use of the simple method described by Nichols[1] in 1896. Nichols showed that the stenosis was similar to syndactylism and remediable by the production first of an epithelialized tract laterally in the scarred tissue to which incisions might be made without recurrence of the adhesions. This tract he produced by inserting a silk braid well into the lateral extent of the region of scarring, the suture being tied and left in place about two weeks. Figi[2] modified slightly this procedure by the addition of a small lead weight clamped over the ends of the suture and allowing the suture to cut through itself, requiring a matter of one or two weeks. Then another suture was inserted farther laterally. Ordinarily mechanical dilatation was used subsequently. A small amount of contraction occurs in these cases after the operation.

REPORT OF CASES

CASE 1.—A middle aged white female school teacher was examined at the Sansum Clinic, Santa Barbara, in 1934, because of trouble in the throat and mal-nutrition. Her voice was markedly lacking in nasal resonance. She was a mouth-breather and was thin and poorly nourished. She stated that the throat had been operated on previously

three times for removal of tonsils and tonsillar remnants, and that following the last operation twelve years before she had noticed considerable impairment to nasal respiration. This had increased in severity until expiration through the nose was impossible. The sense of smell was impaired, the throat constantly uncomfortable as a result of mouth-breathing while with colds there was marked discomfort as well as difficulty in removing nasal secretions.

The general physical examination, except for showing the patient to be underweight, gave normal findings. On examination of the throat there was marked scarring of the pharynx. Posterior rhinoscopy was impossible because, except for an opening 5 mm. in diameter, posterior to the uvula, the nasopharynx was closed off from the pharynx by the adherent soft palate. The tissues of the faucial pillars could not be clearly defined as they blended with the wall of the pharynx and the palate. The scar tissue was very dense and the uvula was pulled to the left side by it. A little air could pass the opening on inspiration, but during expiration the uvula acted as a valve to effectively close this aperture. The patient had, ten years before, visited the Mayo Clinic for correction of her trouble, but said that she was unable to remain for treatment. She is then probably one of the untreated cases reported by Figi[2] and not a new case of stenosis of the nasopharynx.

Under local anesthesia with cocain, a silk worm gut suture carrying three lead shot was inserted into the lateral portion of the scarred tissue of the pharynx on each side. This was difficult and somewhat painful because of the density of the scar. The loop was drawn up loosely and the knot tied. The patient was observed for four days afterwards, then had to return home. When seen again six weeks later, she stated that the suture on the left had worked out a few days after she returned home, while the other had remained in place for a month before cutting through the tissues. The result was excellent from her standpoint, and she was entirely satisfied as the voice was normal, respiration and swallowing easier, and she stated that resuturing was unnecessary. On examination the opening into the nasopharynx measured 5x17 mm. This patient was seen again a year later, and the report was the same—that she was very well pleased. The opening had not appreciably decreased.

Comment: The suture would have been more comfortable, if silk or linen had been used. Leaving the loop in the throat as done here may be an advantage over the original Nichols procedure. No dilatation or postoperative care was given, and judging from the result this was unnecessary. The scar tissue in this case was so dense that

Fig. 1. Stenosis of the nasopharynx, scarring of the pharynx. Large tonsillar remnant.

operation under local anesthesia should not have been attempted, but a general anesthetic used.

Case 2.—G. B., a girl, aged 15 years, came to the Nose and Throat Department of the Greens' Eye Hospital, August 12, 1937, because of obstruction in her throat. Seven years previously the tonsils and adenoids had been operated on. A year later the throat became closed and breathing through the nose had become more difficult, and was impossible during sleep and when the patient had a cold. The left side of the throat was often sore. On examination (Fig. 1) the soft palate was blended with and adherent to the pharynx except for an opening 5 mm. in diameter behind the uvula. The left tonsil had been only partially removed; its remnant was 2x2x½ cm. and contained a small abscess, and the scar tissue present in the pharynx and posterior faucial pillar had caused the tonsil fossa to be flattened so that the tonsil itself lay as much against the posterior as the lateral wall of the pharynx. Several heavy bands of scar tissue were present on the left side. The right side of the throat, from the commissure between the jaws to the midline, was an unbroken plane of mucous membrane and scar.

On August 13th under gas-ether anesthesia the large tonsil remnant was removed by scissors dissection. A doubled linen suture on

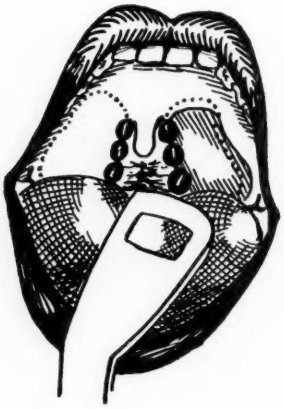


Fig. 2. Following removal of the tonsil. Leaded sutures in place.

which were three heavy lead shot was inserted laterally into the scar of the pharynx on both sides, the opening back of the uvula being used to introduce the sutures into the upper aspect of the scar. The sutures were brought out well below the level of the dorsum of the tongue and firmly tied. The loops of the sutures were made snug, but not tight enough to constrict the tissues. There was little post-operative reaction and no swelling of the uvula or soft palate. (Fig. 2.) The patient returned home the fourth day after operation.

She was re-examined August 24th, when she stated that one suture (left) had worked through on the eighth postoperative day with marked improvement in breathing. The tonsillar fossa was largely healed, but not entirely epithelized, and the opening now measured 20x8 mm. The suture on the right side was about half through the scar tissue. It caused slight discomfort, a pulling sensation.

The patient was next examined September 7. The throat had healed and the opening had contracted slightly so that it measured 5x15 mm. The last suture had worked through a few days after her previous visit. Although much happier because of her ability to breathe and talk more easily, she agreed to have the leaded sutures reinserted. This was done September 7, the patient going home the same day. When last seen a month after the second suturing she stated that the sutures had worked through the scar tissue a week

after being placed in the throat. Healing had occurred and the resulting opening measured 17x17 mm. This she said was entirely adequate and she wished no further treatment.

Comment: The use of leaded sutures for the correction of stenosis of the nasopharynx is a very simple effective procedure which may be quickly and safely performed. Neither of these patients received any post-operative dilatation or other care, and both were well pleased with the result. Although the opening into the nasopharynx was not as large as it is possible to obtain by means of the further use of sutures, it was functionally adequate in both cases. Neither patient lost more than a week from school during the whole period.

BIBLIOGRAPHY

1. Nichols, J. E. H.: The Sequelae of Syphilis in the Pharynx and Their Treatment. Trans. Am. Laryng. Asso., 18:161-168, 1896.

2. Figi, Frederick A.: Stenosis of the Nasopharynx. Arch. Otolaryng., 10:480-490 (Nov.), 1929.

3. O'Connor, Gerald B.: Pharyngeal Reconstruction for Nasophayngeal Stenosis. A New Operative Procedure. ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY, 46:376-386 (June), 1937.

Society Proceedings

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Meeting of Monday, October 4, 1937

THE PRESIDENT, DR. WALTER H. THEOBALD, IN THE CHAIR

The Use of Para-Aminobenzene-Sulphonamide in the Treatment of Streptococcic Carriers

ARCHIBALD L. HOYNE AND JOHN HAYS BAILEY (by invitation)

(Abstract)

Public health control of scarlet fever depends for the most part on the presence or absence of carriers of hemolytic streptococci in the population. In 1934, it was found that among 4,315 scarlet fever patients released from the Municipal Contagious Disease Hospital in an eighteen months' period, there were 190 known carriers responsible for secondary cases of scarlet fever following return to their homes. Thus it is apparent that any treatment that would clear up the carrier state would be a marked advance in control of the disease.

One year ago it was decided to test the efficiency of prontylin because of the reports of its specific action for streptococci. The plan provided for administering the drug to scarlet fever patients during the last quarter of the four week quarantine period. Alternate scarlet fever patients were given one 5-grain tablet of prontylin three times daily between meals. Cultures were made at the end of seven days from the nose and throat of treated patients as well as controls. It was soon evident from examination of cultures that no influence was exerted on the presence of hemolytic streptococci, and the dosage was therefore doubled, each patient receiving 30 grains of prontylin daily.

Of 183 patients, fifty-eight served as controls and 125 received the drug. Among the former group, but seven had negative cultures from the nose and throat at the termination of quarantine. Among the 125 treated cases, thirty-six or 20.8 per cent had negative cultures at the end of the quarantine period. The age distribution of the treated cases is interesting, patients under 7 years of age forming almost 50 per cent of the treated group. The importance of age as a factor in the con-

trol of scarlet fever has been previously referred to, and the removal of tonsils and adenoids before school age should play an important role in lowering the incidence. The largest percentage of negative cultures occurred in the age group over 20 years (ten of seventeen patients). It is the result in this group that makes the figures appear favorable for the drug.

Normally without special treatment from 35 to 40 per cent of patients fail to harbor hemolytic streptococci at the end of four weeks. The apparently favorable results in this series of prontylin treated patients in comparison with untreated patients are undoubtedly due to the small number of patients studied. On the basis of the data presented, it is concluded that irrespective of any value prontylin may have in the treatment of acute streptococcic diseases, it is not effective in the eradication of hemolytic streptococci from the noses and throats of scarlet fever patients at the end of a four week quarantine period.

Blood Cell Response to Sulfanilamide Therapy

JOHN A. BIGLER (by invitation)

(Abstract)

Although sulfanilamide is being very widely used, very little is known of its mode of action. Symptoms of toxicity such as skin rashes, nausea and vomiting, dizziness and hyperpyrexia have been reported during administration of the drug. Cyanosis during therapy has also been mentioned. So far, a survey of the literature shows only relatively few cases of blood cell depression, although there is an undercurrent of feeling that there may occur the same marked depression of the blood elements as is being reported with such drugs as amidopyrine.

Careful observations have been made on ninety-three patients treated with sulfanilamide at Children's Memorial Hospital. With the idea of determining the leukocyte response, daily blood counts and Schilling differential counts were made before, during and after such therapy on a group of thirty-three patients. The leukocyte counts were made at approximately the same hour of the day. A dosage of 15 grains per 20 pounds of body weight was closely adhered to. Of the thirty-three patients, twenty-seven had a leukocytosis and six had a leukocyte count within normal limits when the therapy was started. In both groups there were patients with infection and fever, infection without fever (usually chronic infection) and with no evident infection.

1. *Response when a leukocytosis was present:*

(A) Infection with fever was present in seventeen patients; in seven, a decrease to normal occurred in a crisis-like manner within twenty-four hours after the fever had subsided; in four, the leukocytosis decreased in a lysis-like manner in from one to five days after subsidence of the fever; in six critically ill children who received this therapy for only a short period there was no change.

(B) Three patients in whom an infection without fever was present had a leukocytosis; in two, the leukocytes decreased to normal in a crisis-like manner; the third showed a decrease to normal over a four day period.

(C) A leukocytosis was present in seven patients in whom there was no evident infection; four of them had recently recovered from a throat infection. In four of the seven patients a crisis-like drop to normal occurred within twenty-four to thirty-six hours after medication was started; in two, a lysis-like decrease took place over a period of three days. One patient with a leukocytosis of between 8,000 and 10,000 showed no change in the white cells after five days.

2. *Response when a normal leukocyte count was present:*

(A) Infection with fever. The one patient in this sub-group was given sulfanilamide for two days, when it was discontinued because of vomiting and severe acidosis. There was no therapeutic effect in this instance.

(B) In two of three patients who had infection without fever, the leukocyte count decreased to 4,800, to rise again when the drug was discontinued. These were the only two patients in whom a leukopenia developed. In the third patient there was no change from normal.

(C) No infection was present in two patients with normal white cell counts. In neither was there any change in the leukocyte count during or after therapy.

Not including six patients to whom the drug was not administered until the infection subsided, there were twenty-one cases with a leukocytosis. In thirteen, the leukocytes decreased to normal in a crisis-like manner within twenty-four to thirty-six hours after subsidence of the fever. In seven cases the white cells returned to normal in a lysis-like manner only after forty-eight hours or more, while in one case there was no change. Of six cases with a normal

white cell count, a moderate leukopenia without neutropenia developed in two; in the other four the leukocyte count did not change.

The alteration in the leukocyte response was in the nature of a marked absolute reduction of all the cell elements without any characteristic relative change in the proportion of the different white blood cells as studied by the Schilling count. An increase in the leukocyte count which could be attributed to sulfanilamide did not occur in any case. It did seem, however, as if the drug does cause a depression of the white blood cells and this is borne out by two cases which developed leukopenia and by the spectacularly rapid decrease in the leukocytes as the infection subsided. It seems that the beneficial action of sulfanilamide is due to its own action in the blood stream rather than to its enhancing the power of the leukocytes or increasing their number to control the infection.

In compiling the statistics embodied in this study, a conservative attitude was taken. Consideration was given not only to the individual case being treated but also to similar cases being observed at the same time but not receiving sulfanilamide therapy.

It is concluded that sulfanilamide is an effective therapeutic agent in most hemolytic streptococcus infections. Cyanosis is of frequent occurrence during administration of the drug. There is evidence that sulfanilamide has a tendency to cause a depression of the leukocytes. The action of the drug seems to be independent of the leukocytes in that it does not produce an increase in the total leukocytes or in the proportion of the polymorphonuclear cells. From this study it is apparent that frequent blood cell determinations should accompany sulfanilamide therapy. We have encountered two more cases of leukopenia recently occurring in patients with infection, fever and leukocytosis during sulfanilamide therapy.

Sulfanilamide Therapy

GEORGE S. LIVINGSTON

(Abstract)

This paper analyzes three phases of sulfanilamide therapy: evidence of the clinical value of the drug, especially in otolaryngology; method of its administration, and its untoward and dangerous effects.

Most of the material available for study deals with infections caused by beta streptococcus hemolyticus. Sulfanilamide has also been used in treating other types of infections, with varying results. Certain criteria must be established before judgment can be passed. In the large group of infections which usually terminate favorably, individual cases are valueless. If large series consistently show more

rapid resolution, shorter and milder course, and fewer complications than previous experience has taught us to expect, a strong case in favor of sulfanilamide therapy will be established. Reports already published are sufficiently favorable to encourage continued large-scale study. In the smaller group of infections which have a high mortality, such as streptococcic meningitis, a significant reduction in the death rate establishes the value of the drug much more definitely. The mortality in streptococcic meningitis has apparently been markedly reduced, and it seems probable that future reports will be even more favorable due to more widespread use, earlier administration and a better knowledge of adequate dosage.

Five cases treated with sulfanilamide at the Children's Memorial Hospital were presented. These are typical of a larger group in which a diagnosis of surgical mastoiditis had been made, which by usual standards would have been subjected to operation. All five patients recovered promptly following administration of sulfanilamide. Cases in which parallel results could be expected without the use of the drug, were omitted. In viewing the entire series of hospitalized cases of otitis media and mastoiditis, one has the feeling that a significant advance has been made.

Not all the cases treated with this drug were benefited. The unsuccessful cases divide themselves into two groups. In the first inadequate dosage was given; less than the suggested amounts were used and administration was stopped too soon. The second group comprises seven cases of acute suppurative otitis media in which proper administration of sulfanilamide seemed to exert no beneficial effect. At present the chief value of the drug seems to be infections caused by the hemolytic streptococcus, the meningococcus and the gonococcus; streptococcus viridans and staphylococcus aureus seem to be resistant to its action.

The mode of action of sulfanilamide has not yet been determined. It is probable that it prevents multiplication of the organisms sufficiently to permit the normal defense mechanisms of the body to destroy them. Satisfactory action depends upon the continued presence in the body of an adequate concentration of the drug. Dosage will vary according to the rate of absorption and excretion.

Many derivatives of sulfanilamide and related compounds are being tested experimentally, but most of those reported on so far have proved to be either more toxic or less effective than sulfanilamide. It seems wisest to use only sulfanilamide until some of the newer compounds have been proved conclusively to be superior to it.

From personal experience and from a review of the literature to date, it is concluded that sulfanilamide has already been proved valuable in the treatment of various infections, chiefly those caused by the beta hemolytic streptococcus. Its effectiveness varies with individuals, the stage of illness in which treatment is begun, and adequacy of dosage. Certain unfavorable effects have been noted, most of which disappear quickly on withdrawal of the drug. Of graver significance are reports of methemoglobinemia, sulfhemoglobinemia, acidosis, acute hemolytic anemia, agranulocytosis and optic neuritis. Frequent careful blood studies are of paramount importance. Finally, sulfanilamide should be considered as a valuable adjunct, and not a panacea. All previously accepted means of medical and surgical treatment must continue to be used as indications arise.

DISCUSSION

DR. HOWARD C. BALLENGER: These reports have been confined largely to children. It is possible that in adults we may have a different picture in certain instances if we use this drug extensively. About two weeks ago I was called in consultation by a general physician to see a rather obese woman of about 50, who had concurrently an acute nasopharyngitis; the culture showed hemolytic streptococcus. The blood count was about 8,500. She got along very nicely except for the sore throat, which persisted. The physician gave sulfanilamide in the usual dosage for three days. At the expiration of the three days the blood count was 2,500. At this time when I saw the patient there was a dark spot on one tonsil about the size of a penny. This spot was later covered by a membrane formation. It was the typical bluish-black necrotic area, characteristic of early agranulocytosis. Next morning the blood count was 2,000 and on the opposite tonsil there was a similar area about the size of a pea with a membrane on the uvula and the first tonsil. The next day the blood count was 1,000, later dropping to 500 when death occurred. Whether sulfanilamide was a factor in this case I do not know, but it could be so.

The drug should not be used indiscriminately in mild throat infections, especially in adults.

DR. ALFRED LEWY: The thing we need to know the most about at present is the toxic effects. We have no way, no easy way at least, of determining whether the course of the disease or the result of the drug is producing the symptoms with which we are confronted. I will limit my remarks entirely to treatment of meningitis and other intracranial consequences of otitis media, and as chairman of the committee on meningitis for the Chicago area, I reported to the

American Otological Society last May eight recoveries from cases of hemolytic streptococcus meningitis with positive cultures of the spinal fluid. Eight cases recovered; there were also a number that did not recover. At the County Hospital there were six cases of hemolytic streptococcic meningitis with four recoveries, and I had personal knowledge at that time of four other cases at two other hospitals, with recovery. Dr. Dwyer, Chairman of the New York Committee, reported fourteen cases with recovery. I do not know how many cases he knew of that did not recover. In view of our 97 plus per cent mortality heretofore, this is a very satisfactory showing.

In addition to these cases I would like to mention one I saw recently, a 13-year-old child who had a mastoid operation in May, and went home apparently recovered. Returned to the hospital in August, having had a dizzy spell ten days before. Two days before entrance into the hospital she went into a coma, from which she had come out at the time she entered the hospital, at which time she had a fully developed meningitis, complete paralysis of the muscles of one eye and the internal rectus of the other eye. Hemolytic streptococci was recovered from the blood stream and from the spinal fluid on four different occasions. This child made a recovery. I hope she has recovered. I do not know what will happen to her in the next year.

I would also like to mention three other cases; all three had mastoid operations from ten days to four weeks before I saw them. One entered the hospital with the clinical symptoms of meningitis, and it proved to be a sinus thrombosis. A week later severe occipital headache developed, and a diagnosis was made of posterior fossa lesion on that side, with suspected abscess, but while waiting, the child recovered. The second case was almost identical but without the sinus thrombosis, and there also, while we were watching and waiting, there was a recovery. The third case showed a choked disc and the x-ray report was a definite abscess of the petrous. The petrous did look a little different, but because of the absence of any symptoms except choked disc, we did some watchful wating and the patient is apparently well. I do not know how long they will remain well, but all these cases have occurred in the last six months. They all had sulfanilamide. We have a considerable list of recoveries without operation with sulfanilamide. It has given us courage to do a little watchful waiting, more than we would without it, and in that respect we may have to revise some of our surgical indications.

The intraspinal use of sulfanilamide I have had no experience with. Our dependence was entirely on the use of the drug parenterally or by mouth.

DR. GEORGE SHAMBAUGH, JR.: I would like to report briefly one case. This patient had an acute otitis media on December 4th with marked mastoid tenderness and a temperature of 103 degrees F.

Three weeks later mastoid tenderness was still present with profuse discharge from the ear. For one week there had been increasing pain in the right eye. The diagnosis was early coalescent mastoiditis with probable petrous apex infection. Simple mastoidectomy showed an extensively pneumatized mastoid process. A week after operation sixth nerve paralysis developed on the same side. The pain behind the eye and the sixth nerve paralysis persisted with profuse discharge from the middle ear and the x-ray picture of coalescent petrositis. Because the patient's general condition was good and the symptoms showed a tendency to gradually improve, operation on the petrous apex was deferred.

Four months after the patient was first seen there was still a profuse discharge from the middle ear, the mastoid incision having healed within a few weeks of the operation. The sixth nerve paralysis and the pain behind the eye had also cleared up, but the x-ray picture continued to show a large area of cell destruction in the petrous apex. Sulfanilamide, ten grains three times a day, was begun. Within twenty-four hours the profuse discharge from the ear had stopped and except for a trace of moisture once or twice for the next few days, the ear did not discharge again. The hearing which had been markedly diminished in this ear for four months was normal two weeks later.

DR. T. C. GALLOWAY: We should report all the cases of hemolytic streptococcus meningitis which have recovered after the use of sulfanilamide because that is the best laboratory test we could have. I have never seen a case recover before this year, but since January, I have observed two cases of my own and three at the County Hospital get well and have heard of four other such cases in the Chicago area. One case of mine with marked meningeal symptoms, high cell count, and many organisms, had sulfanilamide and a simple mastoid operation and ran as normal a course as any mastoid. Another, secondary to labyrinthitis, had a labyrinth operation with wide dural exposure and did well with sulfanilamide. When that was stopped after two weeks, there was recurrence which again was controlled by the drug with recovery.

Two cases with definite indications for mastoidectomy cleared up in a few days with dry ears. Twice in cases which did not clear up after the drug, I was struck by the spottiness of the mastoid as if there had been healing when necrosis was not already advanced. It

will be interesting to find out just how much pathology is reversible if this drug can eliminate the infection.

The drug is very new. We all remember that dinitrophenol was hailed as a wonderful cure. I saw a 27-year-old girl who took it two years ago without symptoms until a few weeks ago when she noticed failing vision. Now she has rapidly advancing cataracts. Because we cannot know all of the bad effects of sulfanilamide—especially late effects—I think we shall make a mistake if we use it indiscriminately. It should be saved for the cases in which ordinary methods do not suffice.

DR. M. REESE GUTTMAN: I would like to place on record what I believe to be the first cases of streptococcus hemolyticus meningitis cured in the Chicago area by sulfanilamide. Last March there was admitted on the service of Dr. Sonnenschein in Michael Reese Hospital a girl, three years of age, with a running ear and intermittent temperature for five weeks. Two days prior to admission she became much worse, and on that morning had gone into coma. She was seen at four o'clock in coma, with a stiff neck, and other classical signs of meningitis. Spinal puncture showed streptococcus by smear, several thousand white cells. A positive culture for hemolytic streptococcus was returned later. Through the courtesy of Dr. Sonnenschein I operated on that case at six o'clock that evening, doing an extensive mastoidectomy. The dura was exposed and showed nothing; the lateral sinus was apparently normal. That evening we attempted to get some of the drug. Unfortunately there was none available, but through the courtesy of the DuPont people a supply came by airplane 24 hours later. The girl was still in coma, and received a full dose that evening. She received a large amount of the drug for three days, and came out of the coma, the temperature dropped from 105 to 99 F. and she made an uneventful recovery.

DR. AUSTIN A. HAYDEN: The chairman and secretary are to be congratulated on bringing a most timely and interesting and important subject to the attention of Chicago laryngologists. I think you would be interested to know that the program of the American Medical Association at Atlantic City was held up, so far as publication was concerned, for ten days last year because of some investigation that Helmholst as doing at Rochester. Many interesting things can be said about sulfanilamide. I am informed by Dr. Paul H. Leech of the Council on Pharmaceutics and Chemistry of the American Medical Association that sulfanilamide is quite an old drug. It is the amide of sulphuric acid and has been known from in the sixties or seventies. It was first made in Germany as a dye. For some reason it was not

found to be satisfactory or successful. Unsatisfactory dyes are very frequently turned into medical use. For some reason that amide was neglected for all these years until about 1931, when some experimental work was done on peritonitis in rats, that seemed to offer possibilities.

I was impressed also by a statement made by Dr. Leech. When we talk about the extent to which a drug of this sort will be used, not only because of its worth but because of the publicity—a single drug house shipped to South America in August two tons of sulfanilamide. The price has been enormously reduced. When we talk about the cost of drugs, remember that the first grains of aspirin in the United States cost five dollars a grain, but it is certainly a very cheap and widely used drug at this time.

I think it is well to bear in mind that the Council accepted name is sulfanilamide, not para-aminophenylsulphonamide. I gather from the statistics presented on the board tonight that this drug seems to have a very specific action, not in bone lesions except perhaps in the bones of the head. You will remember that Dr. Bailey showed the effect was nil in osteomyelitis of the tibia. My own experience has not been very satisfactory, but the number of cases I have seen is very limited, and one particular case that I expected to see marvelous results in, made a very prompt death. That case, however, was practically moribund at the time medication was given.

I agree heartily that great care should be used. I fear with the startling reports of successful administration that have been made, it may become a matter of over the counter drugstore prescription.

DR. W. J. NOONAN: The patient I saw had a positive hemolytic streptococcus in the fluid, rigidity of the neck and was given prontosil intramuscularly, prontylin by mouth, sulfanilamide 0.8 per cent solution was given intraspinally.

DR. SAMUEL J. PEARLMAN: There have been recently at Michael Reese Hospital three cases of streptococcus hemolyticus meningitis, all three with positive bacterial findings in the spinal fluid, and all got well on sulfanilamide therapy.

I should like to add my bit to Dr. Galloway's remarks about dinitrophenol. I, too, know of a case wherein the patient took the normal dosage for two days and then almost two years later developed a characteristic dinitrophenol cataract. It is proper, in my mind, to use sulfanilamide in a streptococcus hemolyticus meningitis. No fair-minded person will deny that there has been a great advance in the therapy of that disease. We have had here this evening more reports

of recoveries in the past year than in many years preceding. I am not prepared, however, to fully accept the glowing reports of its efficacy in tonsillitis and mastoiditis. I believe that of the case reports mentioned tonight there is not one of us who cannot match these by similar results in instances where sulfanilamide was not used.

Everyone knows of the child or infant who has a very high temperature due to an acute otitis media; a paracentesis is done, the ear discharges a few hours, the temperature drops and the patient is well. Everyone knows about the instance of mastoiditis wherein preparations for operation are all ready and an obstreperous parent or a delay for one reason or another has resulted in a postponement for a short period of time and, to the amazement of all, a spontaneous recovery.

In the case of a drug such as sulfanilamide where the late results are not known; where each week brings increasing numbers of reports of unfavorable reactions, one should keep an open mind; use it intensively and with a free conscience only in those cases which we know are usually fatal and where much may be gained by therapy, and lastly one should avoid giving it credit for glowing recoveries in diseases which run a self-limited course.

Dr. George T. Jordan: Apparently we have a drug here on which we have sufficient information to go ahead and use it. We certainly must be careful about it, however. I have had three cases where I thought I had to do a mastoidectomy—and cardinal symptoms present and prolonged. In those three cases we gave prontosil hypodermically and they all recovered. I also had a case which parallels that of Dr. Shambaugh, following scarlet fever, in which double mastoidectomy was performed. Trouble persisted on the right side. By the time we wanted to operate again the child had chickenpox. That child got well enough to go home and the ear started up again accompanied by paralysis of the right external rectus muscle and pain behind the eye. The mastoid was reopened and the child made a recovery and has been well for three months. I think we can have sufficient confidence in this drug to use it, if we use it judiciously.

Dr. Paul H. Holinger: We had a similar case on the medical service of the Research and Educational Hospital last March. The patient had an acute severe streptococcic infection of the lung. Bronchoscopy revealed the process to be limited to the posterior division of the left lower lobe, and the secretion aspirated from this area contained a pure culture of hemolytic streptococci. The point in question is that there was an associated low grade nephritis with occasional red cells and casts. The administration of sulfanilamide was followed by an acute exacerbation of the urinary findings, with a shower of

red cells and casts. In view of subsequent work, as well as what Dr. Livingston has told us, we probably should not have given the regular dose of the drug. It was discontinued entirely, however, and the kidney flare-up subsided.

DR. HARRY POLLOCK: I have not much to report in the way of meningitis. Regarding throat infections, I have had two cases recently, one a young man of 27, with a typical streptococcus sore throat. The culture showed hemolytic streptococcus and he had a temperature of 105° F. the first day, and on the second day a temperature of 105.6° F. I started that night on the drug and within twelve hours his temperature dropped to about 99° F. The man was very sick, so sick that they called a medical man. The temperature went up to 102° F. next day and we increased the dose a little bit, and that evening his temperature was normal and has been normal ever since.

I have had two cases like that, streptococcus sore throat, mostly in the pharynx, and both recovered, the temperature dropped within twelve hours and both made a rapid and uneventful recovery. I feel we should use this drug carefully, but there are conditions in which it is indicated and if watched very carefully I think we can avoid any danger. The young man I spoke of was cyanotic before we gave the drug; the temperature was 105.6° F., and within twelve hours the cyanosis disappeared and there was no further trouble.

DR. JOHN A. BIGLER (closing): I would like to say that since we have been interested in the blood cell response during sulfanilamide therapy we have talked to many individuals. One man said he had a case of agranulocytosis which developed as a result of the use of the drug. When the patient died it was found that a leukemia was present. I think one should be careful in describing blood changes because a blood dyscrasia may develop as a result of the disease rather than being due to any therapy.

DR. GEORGE S. LIVINGSTON (closing): I want to say to Dr. Lewy that I do not feel that surgical indications might not have to be revised. I think our indications have been definitely changed by cases which seemed entirely ready for surgical intervention and did not receive it. I meant that in spite of treatment they may still require mastoidectomy. With streptococcic meningitis the patient cannot get any worse, but where we have some means of helping the patient other than the drug, I feel that it is only fair to use it. Nevertheless, if in spite of treatment operation seems indicated it should be done. The danger is not so much with otologists as perhaps other practitioners, not specialists, who have an otologic case, who may adminis-

ter the therapy hoping against hope. I have some figures which I omitted from my talk before because I did not feel it was proper to include such figures in a statistical study. In the nine months ending September 30, 1937, we performed 22 mastoidectomies for mastoiditis; in 1936 over the same period we performed 59; in 1935, 76 in the same period. I do not offer that as proof that sulfanilamide has reduced the number of mastoidectomies, although I feel it had something to do with it. I do not feel it is a large enough figure to draw any conclusions. We know that some years the respiratory organisms in epidemic form are much more severe and virulent than in other years. We know that in the city clinics we must bear in mind the general economic conditions. That may have some bearing on the number of people who come to the clinics. There are fewer now than three or four years ago. That will affect the total number of cases and the number of operations. I am citing that as a possible factor, other than the value of sulfanilamide.

The criticism Dr. Pearlman made I think is entirely valid. I tried to be careful to eliminate that type of case and I realize that the few I put in were not above criticism because we all know of cases where we felt operation was imminent, and was postponed for some reason, and the patient got well without sulfanilamide. That criterion can only be applied in very large groups. If large clinics will continue to record their experiences year after year, perhaps we will have in three or four years such a body of evidence that it will be incontrovertible, but if we save one case here and one there, it will not mean anything.

Books Received

The Endocrines in Theory and Practice.

Articles by Various Authors Republished from the British Medical Journal with a Preface by the Editor. Cloth, Crown 8vo of 278 pages. Philadelphia, P. Blakiston's Son & Co., Inc., 1937. Price, $3.50.

A very absorbing and timely book is this small monograph on the subject of endocrines which has just appeared. The book is made up of twenty-eight articles which appeared in the British Medical Journal from October 17, 1936, to May 15, 1937.

They were contributed to that journal by invitation and constitute a complete and concise review of the ductless glands, a subject in which, to quote the compiler, "enthusiasm outran knowledge."

The present work effectively selects what has been demonstrated over a decade to be fact and arranges it in complete and easily accessible form.

Such a book as this is peculiarly serviceable to the specialist who, familiar with the literature of his own subject, is often at a loss to co-ordinate his information on a general medical subject such as this from the works at his command.

Diseases of the Ear, Throat and Nose.

By J. Douglas McLaggan, M.A., M.B., F.R.C.S. Eng. and Edin. Surgeon in Charge of the Ear, Nose and Throat Department, Royal Free Hospital. Surgeon, Central London Throat, Nose and Ear Hospital. Surgeon in Charge of the Ear, Nose and Throat Department, Croydon General Hospital. Cloth, Demy 8vo of 338 pages, with 9 plates and 135 illustrations. London. H. K. Lewis & Co., Ltd., 1937. Price, 15s. net.

This book has little to recommend it. A very superficial presentation of material which has been so adequately and compactly handled so many times before.

Notices

The American Board of Otolaryngology

An examination was held in Chicago, October 8th and 9th, 1937, prior to the meeting of the American Academy of Ophthalmology and Otolaryngology. One hundred and one candidates were examined—of this number seventy-nine were certified.

An examination will be held in San Francisco, June 10th and 11th, 1938, prior to the meeting of the American Medical Association.

Prospective applicants for certificate should secure application blanks from the secretary, Dr. W. P. Wherry, 1500 Medical Arts Building, Omaha, Nebraska.

H. P. Mosher, M.D., President
W. P. Wherry, M.D., Secretary.

Advisory Board for Medical Specialties

The Advisory Board for Medical Specialties adopted the following resolution at its meeting in Atlantic City on June 6, 1937:

> Resolved, That the President appoint four members of the Advisory Board for Medical Specialties with power to add to their number and to form a Commission on Graduate Medical Education to study the problems of graduate and postgraduate medical training, such a Commission to be comprised of representatives of the medical profession, the hospitals, the universities, the medical schools, and the licensing bodies.

In keeping with that action a Commission on Graduate Medical Education has been created, the personnel of which follows:

Fred L. Adair, Chicago, Vice-President, American Board of Obstetrics and Gynecology.

A. C. Bachmeyer, Chicago, Director, University of Chicago Clinics; Former President, American Hospital Association.

Donald C. Balfour, Rochester, Director, Mayo Foundation; Member, Board of Regents, American College of Surgeons.

Kenneth D. Blackfan, Boston, Professor of Pediatrics, Harvard Medical School.

James D. Bruce, Ann Arbor, Vice-President and Director of Department of Postgraduate Medicine, University of Michigan; Chairman, National Committee on Postgraduate Medical Training.

R. C. Buerki, Madison, Superintendent, University of Wisconsin Hospital; Former President, American Hospital Association.

Anton J. Carlson, Chicago, Professor of Physiology, University of Chicago.

Walter F. Donaldson, Pittsburgh, Secretary, Pennsylvania State Medical Society and former member of Council on Medical Education and Hospitals of American Medical Association.

Reginald Fitz, Boston, Member, American Board of Internal Medicine; Member, Council on Medical Education and Hospitals.

Evarts A. Graham, St. Louis, Chairman, American Board of Surgery.

F. W. Hartman, Detroit, Secretary-Treasurer, American Board of Pathology.

Willard C. Rappleye, New York, Dean, Columbia University Faculty of Medicine; Director, New York Post-Graduate Medical School; Former Director of Study, Commission on Medical Education.

J. Stewart Rodman, Philadelphia, Secretary, American Board of Surgery; Medical Secretary, National Board of Medical Examiners.

Harold Rypins, Albany, Secretary, New York State Board of Medical Examiners; Former President, Federation of State Medical Boards of United States.

Alfred Stengel, Philadelphia, Vice-President in Charge of Medical Affairs, University of Pennsylvania.

William P. Wherry, Omaha, Secretary, American Board of Otolaryngology; Executive Secretary, The American Academy of Ophthalmology and Otolaryngology.

Allen O. Whipple, New York, Vice Chairman, American Board of Surgery; Member, Committee on Graduate Teaching, American Surgical Association.

Ray Lyman Wilbur, Stanford, President, Stanford University; Chairman, Council on Medical Education and Hospitals of the American Medical Association; Former President, American Medical Association; Former President, Association of American Medical Colleges.

John Youmans, Nashville, Director of Postgraduate Instruction, Vanderbilt University School of Medicine.

November 1, 1937.

The Commission will undertake to mobilize current opinions as to how the problems in this field can best be solved and to formulate

the educational principles involved in graduate and postgraduate medical training. It is hoped that standards of training can be drawn up which will be of help to the Council on Medical Education and Hospitals and other agencies concerned with the inspection and evaluation of the facilities needed. There will be no duplication of effort nor conflict with the Council and these other agencies. The results of the studies by the Commission should be of real assistance to the specialty boards, the medical profession, hospitals, medical schools, state boards of medical examiners, and other institutions and organizations concerned with this phase of American medicine.

Casselberry Prize Fund

The sum of $500.00 having accrued from the Casselberry Fund for encouraging advancement in the art and science of Laryngology and Rhinology, said sum is now available, in part or as a whole, for a prize award, decoration, or the expense for original investigation or research in the domains mentioned above. Theses or reports of work must be in the hands of the Secretary, Dr. James A. Babbitt, 1912 Spruce Street, Philadelphia, before February 1st of any given year.

Abstracts of Current Articles

NOSE.

Reconstruction of the Flat Nose (Metodo personal parala correcion de la nariz aplastada).

Loza, M. Ganzalez (Rosario), Rev. Arg. de O. R. L., 6:147 (May-June), 1937.

Using a trans-columellar and subalar V-shaped incision, the alar cartilages are uncovered laterally, brought up back to back in front of the triangular cartilage, sutured together with fine catgut, and thus build out the nasal tip and lower part of the bridge. Silk skin sutures, filiform drainage and a plastic bandage for 48 hours produce much better results for Gonzalez Loza than previous experiments with transplant or foreign body grafts.

FENTON.

Stimulation of the Nasal Mucosa; Its Physiologic Effects (De l'attouchement de la muqueuse nasale par stylets, et de quelques uns de ses effete physiologiques).

Maur, J. F. (Paris), Rev. de L. O. R., 58:655 (June), 1937.

This is an interesting historical review of the subject of sensitive zones on the turbinates (sympathicotherapy), formerly practiced by Bonnier, lately by Leprince and Koblanck.

Using dull metal applicators, the author notes the following physiological effects:

1. Naso-facial reflex (lacrimination, conjunctival congestion).

2. Diminished reaction of blood pressure during epigastric compression.

3. Diminished reaction of pulse rate increase on injection of one milligram of atropin.

4. No effect on blood calcium.

5. No effect on alkaline reserve.

These reactions only last a few minutes and are probably dependent on parasympathetic responses. While certain asthmatics or sufferers from vasomotor troubles may be helped, the author is skeptical about any cures of distant organs by this method of "reflex therapy."

FENTON.

Significance of Osseous Changes of the Middle Turbinate in Nasal Polyposis (Sul significato delle alterazioni ossee del turbinato medio nella poliposi nasale).

Mesolella, V. (University of Naples), Arch. Ital. di Otol., Rino and Laring., 49:22 (Jan.), 1937.

Mesolella reviews briefly the pathogenesis of nasal polyps, describes histopathological findings of the bony framework in ten cases of nasal polyposis and presents six photomicrographs of the middle turbinate.

He believes that rarefying osteitis found in the middle turbinate, in most cases of polyposis, is a secondary or final stage of the inflammatory process of the turbinate. This he explains by the fact that, in some cases of nasal polyposis, he observed inflammatory reaction in the mucosa and periostium, also destruction of periostium and rarefying osteitis; in others, invasion of the mucosa, periostium and erosion of the latter only in some areas, but no evidence of osteitis; and finally, in other cases there was no evidence of alteration in the periostium nor bone, but only an inflammation of the mucosa.

Therefore, he believes that if osteitis rareficans was the etiological factor, the bony changes should have been found in all cases of nasal polyposis.

SCIARRETTA.

PHARYNX

Unrecognized Complications Secondary to Peritonsillar and Lateral Pharyngeal Abscess, With Case Reports.

Porter, Charles T. (Boston), Arch. Otolaryng., 26:127 (Aug.), 1937.

In too many cases of peritonsillar or lateral pharyngeal abscess complications are unrecognized or inadequately operated on.

The pharyngo-maxillary fossa is most important. It lies in a key position and is to the deep infection of the neck, leading to infection of the blood stream as the ethmoid bone is to the sinusitis and orbital infection.

Cultures of blood are not to be depended on, as the results are negative in a majority of the cases reported. Cultures should be grown both aerobically and anaerobically in all cases, and doubtless a much higher percentage of positive cultures would be found.

In all cases in which there is definite thickening of the vein or a thrombus obliterating the vein up to the jugular bulb, the mastoid should be opened and the sigmoid sinus explored. I am convinced

that a great many of the secondary complications, such as septic emboli, are liberated through the petrosal veins and the torcular to the general circulation from an infected sinus above the jugular bulb.

TOBEY.

Nasopharyngeal Abscesses and Cysts.

Woodward, Fletcher D. (University, Va.), Arch. Otolaryng., 26:38 (July), 1937.

A summary of 14 cases reveals the following: All the lesions occurred in young adults. Four of them were retention abscesses of the median cleft of the pharyngeal tonsil. Ten were retention abscesses of the pharyngeal bursa and presented on inspection a smooth bulging surface, yellowish or white, situated high up in the nasopharynx and usually a little lateral to the midline. They were from 1 to 2 cm. in diameter, and their retained secretions were under sufficient pressure to produce a taut anterior surface. Postnasal discharge, sore throat and cough were the symptoms in four cases, deafness and tinnitus in five, post-cervical pain and adenitis in one, otalgia in three, a sense of soreness in the nasopharynx in three and focal disease, with no localizing symptoms in one.

The diagnosis is readily made by examination with mirrors, provided sufficient time and mirrors of various sizes and angles are used.

The treatment has been the surgical removal of the anterior wall with a punch forceps, working either through the mouth under direct vision or through the nose.

The origin, pathology, frequency and symptomatology have been well covered in the articles referred to in the footnotes.

TOBEY.

LARYNX

Prognosis in Laryngeal Tuberculosis.

Greene, Jos. B. (Asheville, N. C.), Arch. Otolaryng., 26:18 (July), 1937.

It is worthy of note that the mortality from tuberculosis has been reduced to about one-third of what it was thirty years ago.

It cannot be questioned that the situation and the type of the lesion of the larynx have an important bearing on the prognosis. Lesions situated on the posterior commissure or on the vocal chords offer the most favorable prognosis, and fortunately these are the situations in which the lesion is more frequently encountered. In tuberculosis, as in cancer, the intrinsic lesions in these locations offer

a more favorable prognosis than those which appear on the epiglottis, the ary-epiglottic folds or the arytenoid cartilages. The unfavorable prognosis in these cases is due not only to the more painful nature of the lesion, which interferes with nutrition, but to the difference in the type of tissue involved. Four types of laryngeal lesion are recognized—infiltration, ulceration, perichondritis and tuberculoma. It is obvious that these types often merge into each other. Pseudo-edema is noted at times, involving chiefly the arytenoid cartilages and the epiglottis. This type of lesion is usually painful, and from its very nature adds to the gravity of the prognosis. Multiple lesions of the larynx are more serious than those in which the tubercle appears at a single site. For instance, a tuberculous process appearing on both sides of the larynx is more serious than a lesion confined to one side. Perichondritis of the epiglottis or the arytenoid cartilages offers an unfavorable prognosis, and when a pale edematous swelling in this region is noted the prognosis becomes well nigh hopeless. It is thought that this type of lesion is often due to an infection of the blood stream, as distinguished from the intrinsic lesions, which are believed to arise from contact with sputum. It is well to bear in mind that there is a strong tendency for the lesion in the larynx to be of the same type as that found in the lungs; that is, when there is an exudative type of involvement in the lung, one can expect an ulcerative type in the larynx, and when there is a fibrotic type in the lungs, there is likely to be fibrosis in the larynx, with healing tendencies. To this, however, there are many exceptions.

The sedimentation rate should be taken, for it is now regarded as a fair measure of the patient's resistance to the infection.

The author discusses age, sex, other lesions in the body, pneumothorax, removal of diseased tonsils, electrocautery and the possible danger of section of tuberculous lesions of the larynx.

TOBEY.

Care of the Vocal Cords in Singers and Speakers.

Rees, Sir Milsom (London), Brit. Med. J. (July 31), 1937.

Under the general question "What is singing?" the author classifies the sound production of different voices as follows:

	Vibrations per Second	Average Wave Length
Bass	87-256	12 ft.
Baritone	106-341	
Tenor	128-435	6 ft.
Contralto	160-512	3 ft.
Mezzo-soprano	192-640	
Soprano	Up to 768, occasionally higher	1½ ft.

The beauty and carrying power of the voice depends upon the proper posing of the voice to use to best advantage the resonators of the upper air spaces and upon the cords having fine elastic tissues. Anything which may interfere with the sharp edge of the vocal cords, such as bad tuition, over-stretching of the elastic fibers or any other irritants, may injure the voice.

The interesting observation is advanced that since the aeroplane enables the tenor to fly from one country to another in time for rehearsal, the day before the advertised performance, he is now subjected to sudden changes in temperature and humidity which give rise to laryngeal changes. The laryngologist is confronted with the problem of getting the artist through his performance as best he may in the minimum space of time. Certain sprays are recommended for this purpose.

This author advises against tonsillectomy in the case of established artists. He suggests that tonsil operations will inevitably bring about some alteration of the voice, and when deterioration of the voice eventually occurs, as it does naturally, it is likely that the surgeon will be blamed. Contrary to the usual opinion, this author feels that deviated septa, save in unusual cases, should remain untouched.

The Cartilaginous Framework in Malignant Tumors of the Larynx (L'apparato cartilagineo nei tumori maligni della laringe).

Ricci, F. C. (University of Milan), Arch. di Otol., Rino. and Laring., 48:581 (October), 1936.

Twenty-three cases of laryngeal carcinoma were studied by the author, to determine the possible histopathological changes occurring in the cartilaginous structures of this organ. These investigations demonstrated the extension reached by the tumor and the alterations produced by it in the laryngeal tissues. It is of interest to note that in 70 per cent of his cases, even though the malignant process was far advanced, the cartilaginous framework was not involved.

A small lesion, of recent date, affecting only the mucosa, caused inflammatory reaction in the submucosa and, to a small degree, in the perichondrium.

Cases in which the cancerous growth invaded the soft tissue without penetrating the perichondrium, the latter manifested evidences of a tenacious fight against the neoplastic attack with lymphocytic infiltration, connective tissue hyperplasia, increase in number of blood vessels, etc. Therefore, the perichondrium became very thick not only immediately beneath the neoplasm but for some distance until it gradually thinned out.

In other cases the neoplastic cells had broken through the perichondrium and penetrated the cartilage. Here a perichondrial reaction was distinctly seen at the immediate vicinity, while in other instances this collagenous fascia showed no defensive reaction whatever.

The cartilaginous lesion was also produced by vascular metastasis. In these specimen the perichondrium was thickened, but neither destroyed nor invaded by the neoplasm, yet the cartilage was attacked extensively by the malignant process. This was exhibited by neoplastic masses in the blood vessels passing through the cartilage. These malignant cells could be seen breaking through the vessel wall and spreading into the cartilaginous tissue.

Another type of neoplastic invasion of the cartilage was seen in regions where the retrogressive and degenerative senile changes occurred. In areas where ossification was taking place the neoplastic cells made their way in between the trabeculae, invading the marrow spaces, and thus spreading throughout the cartilage.

Finally, when the malignant process was far advanced, the cartilagenous structures were so extensively involved and altered that it was difficult to find and recognize the normal tissue.

Five microphotographs accompany this article.

SCIARRETTA.

EAR

Critique of the Present Treatment of Deafness Due To Lesions in the Conduction Mechanism.

Friesner, Isidore and Druss, J. G. (New York), Arch. Otolaryng., 26:259 (Sept), 1937.

The authors present the pathologic changes which occur in inflamed or infected ears, and point out that the anatomic state of the tympanic cavity is also an important factor in the end-results of the process of repair. The effect of the presence of embryonic tissue in the tympanum is discussed.

In discussing the treatment of chronic progressive deafness they concern themselves with the use of the eustachian catheter to condemn it.

They have nothing to offer as a constructive substitute in therapy, but emphasize preventive measures.

There is an excellent discussion by Dr. Edward H. Campbell of Philadelphia and Dr. John Randolph Page of New York, who disagree largely with the author.

TOBEY.

Vestibular Troubles Associated with Cranial Trauma (Ápropos des troubles vestibulaires dans le syndrome post-commotionel).

Portmann, G., and Despons, J. (Bordeaux), Rev. de L. O. R., 58:585 (June), 1937.

Twenty of thirty-six cases of recent head injury showed hyperexcitability to vestibular tests, nine were normal and seven subnormal. These troubles are a part of the concussion syndrome, and their variability depends on the degree of interference with the intracranial circulation and nervous pathways. They may appear late and last a long time. They are rarely associated with cochlear troubles, unless petrous fracture occurs.

FENTON.

MISCELLANEOUS

A Study of Diet in Relation to Health. Dark Adaptation as an Index of Adequate Vitamin A Intake. Technique and Preliminary Results.

Mutch, J. R. and Griffith, H. D. (Aberdeen), Brit. Med. J. (Sept. 18), 1937.

The authors present their method of testing fatiguability of the retina as an index of vitamin A content in the blood. The apparatus differs somewhat from those available in this country and the method of recording findings results in a definite type of curve. The work is presented in some detail.

The authors have established a limit below which all subjects react with improved adaptation to the demonstration of vitamin A. Those whose first reaction is above this limit do not respond to vitamin A.

Index of Authors

Index of Titles

VOL. 46 DECEMBER, 1937 NO. 4

ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY

FOUNDED BY JAMES PLEASANT PARKER

Published Quarterly

BY THE

ANNALS PUBLISHING COMPANY

7200 WYDOWN BOULEVARD

ST. LOUIS, MO., U.S.A.

ANNUAL SUBSCRIPTION IN UNITED STATES, SPAIN, CENTRAL AND SOUTH AMERICA, $6.00 IN ADVANCE. CANADA, $6.40. OTHER COUNTRIES, $6.80

THE ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY
Published Quarterly by
THE ANNALS PUBLISHING COMPANY, 7200 Wydown Boulevard, St. Louis, U. S. A.
Entered at the Postoffice, St. Louis, Mo., as Second-class Matter.

THE ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY is published quarterly by The Annals Publishing Company, 7200 Wydown Boulevard, St. Louis, Missouri. Subscriptions and all communications of a business nature should be sent to this address. Manuscripts for publication should not be sent to this office.

The subscription price in United States, Spain, Central and South America is $6.00 per annum payable in advance; $6.40 in Canada, and $6.80 in all other countries of the postal union. Single copies may be had at the rate of $1.50 each. Unless otherwise specified, subscriptions will begin with the current number.

In notifying this office of change of address, both the old and the new address should be given.

Information for contributors will be found on the inside back cover.

THE ANNALS OF OTOLOGY, RHINOLOGY AND LARYNGOLOGY
Published Quarterly by
THE ANNALS PUBLISHING COMPANY, 7200 Wydown Boulevard, St. Louis, U. S. A.
Entered at the Postoffice, St. Louis, Mo., as Second-class Matter.

TO CONTRIBUTORS:

Original articles and all other material intended for publication, also exchanges and books for review, should be directed to Dr. Arthur W. Proetz, 1010 Beaumont Bldg., St. Louis, Mo.

The ANNALS may accept for publication original communications relating to otolaryngology and its borderline subjects, case reports, abstracts, book reviews and such letters and announcements as may be of interest to its subscribers at large. While a reasonable inquiry is made into the standing of authors and the authoritativeness of their statements, the editors and publishers can assume no responsibility for them.

Articles are accepted for publication only with the understanding that they appear in no other journal. This does not apply to their inclusion in the published transactions of the various societies.

Manuscripts should be typewritten, on one side of the paper only. They should be double spaced and widely marginated. If the material was presented before a scientific body, a footnote should indicate its name and the place and date of the presentation. Manuscripts should be revised and corrected for spelling, punctuation and grammar. The telegraphic style, omitting articles and conjunctions, sometimes employed for hospital records, is not acceptable for published articles.

References to other published articles must be complete and the data should be set down in the following, now commonly accepted order: author's surname, initials, title of article, journal, volume, page, month and year.

Illustrations essential to the text will be published without cost to the author, but the editors reserve the right to delete illustrations. These, to be acceptable, must be of first quality. Photographs, wash drawings, and shaded pencil drawings are reproduced by means of half-tone plates. Line drawings to be reproduced as zinc etchings must be in black ink on white paper. Colored ink, blue quadrille rulings and pencil marks in such drawings (except in rare cases) and photographs of charts or other printed matter are not acceptable. Unless the artist's lettering is of the first quality it is preferable to carry reference lines to the margin of the drawing and to have us set the lettering in type. When it is necessary for the sake of clarity to mount several illustrations together, authors are cautioned to bear in mind the proportions of our pages and to mount them accordingly. Each illustration should have written (not clipped) on its back (1) the author's name, (2) the title of the paper, (3) the number of the illustration, and (4) the legend; (5) the *TOP* should be clearly indicated. Elaborate tables are likely to be confusing. It is usually preferable to substitute several smaller ones.

Proofs will be sent to authors in ample time for correction. If these are not returned, the articles will be printed as corrected by our readers. These are hand proofs and do not indicate the quality of half-tone plates. Authors should see that plates correspond to their legends and that their tops are uppermost. (This is especially important with photomicrographs.)

One hundred reprints are furnished gratis to authors, but these will be sent only if specifically ordered on the blank which accompanies proofs. Extra copies may be had at prices quoted on this sheet. Orders must be signed by the author in person.